001-S

SELF-REPORTED DIABETES AND MORTALITY IN A PROSPECTIVE CHINESE ELDERLY COHORT STUDY IN HONG KONG. *Chen Shen, C Mary Schooling, Wai Man Chan, Siu Yin Lee, Tai Hing Lam, Gabriel M Leung (The University of Hong Kong, Hong Kong SAR China)

In the West, diabetes mellitus is associated with a higher mortality rate from all and specific causes including cancer, cardiovascular and respiratory diseases. However, this association is unclear among non-Western populations where the pattern of diabetes is different, i.e., high rates of diabetes in relatively non-obese populations often with low rates of ischemic heart disease. The authors examined the association of diabetes with all-cause and cause-specific mortality using a large prospective non-Western cohort of older people. Multivariable Cox regression analysis was used to assess the adjusted associations of self-reported diabetes with death from all-cause and specific causes, using a population-based prospective cohort of 66,820 Chinese aged 65+ years enrolled from July 1998 to December 2001 at all the 18 Elderly Health Centers of the Hong Kong Government Department of Health, and followed until May 30, 2012. During ten-years of follow-up 19,845 deaths occurred. Self-reported diabetes was associated with a higher risk of death from all-causes (hazard ratio (HR) = 1.42, 95% confidence interval (95% CI) 1.37, 1.48), cardiovascular diseases (HR = 1.59, 95% CI 1.48, 1.70), infectious diseases (HR = 1.90, 95% CI 1.52, 2.38), renal diseases (HR = 2.47, 95% CI 2.13, 2.87), ischemic heart disease (HR = 1.90, 95% CI 1.71, 2.11), stroke (HR = 1.49, 95% CI 1.29, 1.72) and pneumonia (HR = 1.40, 95% CI 1.25, 1.57), adjusted for age, sex, socio-economic position (education and monthly expenditure), lifestyle (smoking, alcohol use, physical activity and body mass index) and self-reported health status (comorbidities). Similarly adjusted, self-reported diabetes was only weakly associated with death from cancer (HR = 1.09, 95% CI 1.00, 1.18) and respiratory diseases (HR = 1.10, 95% CI 0.99, 1.21). A different pattern of associations of diabetes with mortality in a different population suggests the drivers of diabetes onset may be contextually specific.

002-S

ALCOHOL USE AND DEATH FROM RESPIRATORY DISEASES: A PROSPECTIVE CHINESE ELDERLY COHORT STUDY. *Chen Shen, C Mary Schooling, Wai Man Chan, Siu Yin Lee, Ping Sum Ng, Tai Hing Lam (The University of Hong Kong, Hong Kong SAR China)

In Western settings, moderate alcohol use is associated with a lower risk of death from respiratory diseases. However, moderate alcohol use is socially patterned, making this association vulnerable to contextual biases. Evidence from other contexts where the typical drinking pattern is different may clarify such observations. Multivariable Cox regression analysis was used to assess the adjusted associations of alcohol use (never, occasional social (<1/week), weekly social, moderate (regular drinking of <210g ethanol/week for men and <140g ethanol/week for women), excessive, (regular drinking of >moderate amounts), and former) with death from respiratory diseases using a large, population-based cohort of older people. Esophageal cancer was used as a validation outcome because alcohol causes esophageal cancer. After a mean follow-up of 9.3 years, 3064 deaths from respiratory diseases occurred. Most current alcohol users were occasional social drinkers (<1/week). Moderate alcohol users had a lower risk of death from respiratory diseases, but had a higher risk of esophageal cancer, adjusted for age, sex, socioeconomic position, lifestyle and health status. Occasional social drinking (<1/week) was associated with a lower risk of death from respiratory diseases, but not with esophageal cancer. The typical drinking pattern, i.e. occasional social drinking, which is unlikely to have any biological effect, was similarly associated with a lower risk of respiratory diseases as moderate alcohol use, suggesting the attributes of being a typical drinker may be protective.

003-S

THE TRAJECTORY OF COGNITIVE FUNCTION AND THE ASSOCIATED SOCIAL AND PHYSICAL DETERMINANTS IN THE ELDERLY OF TAIWAN. *Ting-Yu Chen (National Defense Medical Center, Taiwan)

Objectives: This study aimed to understand the trajectory of cognitive function and the related physical and social factors of the elderly in Taiwan. Method: Data are from the Taiwan Longitudinal Study on Aging (TLSA), a nationally representative study first conducted in 1989. A total of 2763 adults older than 65 years, followed for 15-year in five waves between years 1993-2007 were included in the analysis. The cognitive function was measured by the Short Portable Mental Status Questionnaire (SPMSQ). Group-based trajectory analysis was applied to identify distinct trajectories. Generalized Estimating Equations (GEE) was used to estimate the factors associated with cognitive trajectories. Results: The group-based trajectory model classified individuals into 3 groups based on their cognitive function, namely continuous high, high-decline, and low-decline. The continuous high group was younger, more males, with higher education, exercised more, higher prevalence of smoking and using alcohol. They also rated their health as good with lower prevalence of diabetes, depression symptoms, less problem in ADL, IADL, and mobility tasks. They had better social and emotional support. Longitudinal analysis indicated that BMI, health status, physical function, depression, and social support may be the potential risk factors associated with cognitive function. Conclusion: The trajectory showed that the low cognitive function occurred in very early stage (<65 years old). Prevention and screening should begin early to delay the deterioration.

004-S

IMPACT OF CAREGIVING TRANSITIONS ON PERCEIVED STRESS IN 990 OLDER WOMEN IN THE CAREGIVER STUDY OF OSTEOPOROTIC FRACTURES (CG-SOF). *Jennifer Lyons, Kristine Ensrud, Teresa Hillier, Lisa Fredman (Boston University School of Public Health, Boston MA 02115)

Caregiving is stressful and varies in intensity over time. Greater caregiving intensity is associated with increased stress, but the relationship between transitions in caregiving intensity and stress remains unclear. We evaluated the associations between transitions into and out of caregiving, and between caregiving intensity levels, on Perceived Stress Scale (PSS) scores following the transition among 990 women (mean [m] age = 81) from CG-SOF who participated in up to five interviews from 1999-2009, given at approximate annual intervals. Caregivers (CGs) were defined as those who assisted someone with one or more basic or instrumental activities of daily living (ADL/IADLs), and were categorized as high- or low-intensity using the sample-based median number of ADL/IADL tasks they provided (1 and 4, respectively). Analyses were performed on participants with data on caregiving and PSS at two consecutive interviews, resulting in 2673 transitions. Among participants whose caregiving intensity level remained constant over two interviews, high-intensity CGs reported the highest stress, adjusted for confounders (m = 19.1, standard deviation [sd] = 0.5), followed by low-intensity CGs (m = 16.8, sd = 0.6) and non-caregivers (NCGs) (m = 15.8, sd = 0.2) ($p < 0.01$). Those who ceased caregiving reported similar stress levels as continuous NCGs, except for NCGs who provided care for a brief period during the interval ($p = 0.06$). NCGs who transitioned into either high- or low-intensity caregiving reported similar stress levels as each continuous caregiving group, respectively. These results highlight the importance of evaluating both caregiving status and intensity longitudinally to effectively control for the dynamic nature of caregiving over time.

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005-S

INFLAMMATORY BIOMARKERS AND GLOBAL COGNITION: THE GINKGO EVALUATION OF MEMORY (GEM) STUDY.

*Monisha Sharma, Annette Fitzpatrick, Gloria Chi, Oscar Lopez, Nancy Jenny, Steven DeKosky (University of Washington School of Public Health, Seattle WA 98195)

With the aging of the population and increased longevity, preventing cognitive impairments has become a major public health concern. Research suggests inflammatory biomarkers may serve as early predictors of cognitive impairments and dementia since these diseases involve vascular as well as neurodegenerative components. We examined the association between four inflammatory biomarkers (Pentraxin-3 (PTX3), Endothelin-1 (ET-1), Serum Amyloid Protein (SAP), and RAGE) and global cognitive function as measured by the Modified Mini-Mental State Examination (3MSE) in 1,315 elderly participants from the Ginkgo Evaluation of Memory (GEM) Study. Participants free from dementia at baseline were evaluated every 6 months over 7 years and censored for dementia and mortality. Participants completed an average of 10.4 3MSE tests. Baseline biomarkers were modeled using generalized estimating equation (GEE) regression with linear interpolation and inverse probability weighting. After controlling for demographics and cardiovascular risk factors, only PTX3 was significantly associated with decline in the 3MSE, with each increase in standard deviation of PTX3 associated with a 0.48 decrease in 3MSE score (95% CI 0.18-0.77). Adjustment for APOE genotype slightly attenuated the association, although it remained statistically significant. ET-1 and RAGE were also inversely related to mean 3MSE score while SAP was found to be protective, although none of these associations were statistically significant. The results suggest that PTX3 may be a useful indicator for identifying individuals at high risk of cognitive decline and for targeting early treatment and prevention therapies.

006

PROGRESSION OF MOBILITY LIMITATIONS IN OLD AGE: THE COMBINED EFFECT OF MOBILITY-RELATED FATIGUE AND SOCIO-ECONOMIC POSITION.

*Charlotte Nilsson, Volkert Siersma, Minna Manty, Rikke Lund, Mikkel Vass, Kirsten Avlund (Institute of Public Health, University of Copenhagen, Copenhagen K Denmark)

Mobility-related fatigue predicts mobility limitations and disability in old age. Social inequality in disability is well known, but the interplay between socio-economic position (SEP) and mobility-related fatigue is unknown. The aim of this study was to assess the combined effect of mobility-related fatigue and SEP on mobility decline among older Danes. 2874 individuals without mobility limitations enrolled in the Danish Intervention Study on Preventive Home Visits constituted the baseline population. Questionnaire-data were obtained at baseline in 1998/1999 and at follow-up at t = 1.5, 3 and 4.5 years. Data on SEP were register-based. Self-reported mobility limitations were assessed as the number of mobility activities performed without need of help (range 0-6). Multivariate linear regression models using generalized estimating equations were performed, adjusted for differential drop-out. Regression coefficients represented the mean difference in number of mobility limitations when compared to the joint reference category of those in high SEP and without fatigue (negative coefficient = more limitations). Analyses were stratified by baseline-age (75 or 80 years), adjusted for gender, mental well-being, home help, expenses for medication, physical activity and social relations. For the 80-year-olds the mean difference in number of mobility limitations between the joint reference category and individuals in low SEP without fatigue at t = 3 was -0.41 (95% confidence interval -0.73;-0.10). Fatigue predicted mobility decline with a mean difference in number of mobility limitations from the joint reference category of -0.52 (-0.76;-0.27) among those in high SEP and -1.00 (-1.48;-0.53) among those in low SEP. Similar tendencies were found at all follow-up assessments in both age groups. Fatigue and low SEP are both risk factors for mobility decline over time in old age. There appears to be no synergy-effect between these two risk-factors on mobility decline.

007

LIFE SPACE AND COGNITIVE DECLINE: INDEPENDENT OF MOBILITY AND PHYSICAL, SOCIAL, AND COGNITIVE ACTIVITY?

*Bryan James, Aron Buchman, Patricia Boyle, David Bennett (Rush Alzheimer's Disease Center, Chicago IL 60612)

We have shown that a larger life space—the extent of movement through the environment beyond the home—is associated with slower decline in cognitive abilities. However, we have also shown that many related constructs are also related to cognitive decline including mobility as well as physical, social, and cognitive activities; it is unclear whether the life space-cognitive decline association is independent of these better known predictors. In this longitudinal analysis, we examined the independent associations of each of these constructs with cognitive function and decline in 673 participants of the Memory andAging Project. Life space (ranging from home to out of town) in the previous week, and level of participation in social and cognitive activities were measured through self-report. A composite mobility performance score was based on four performance tasks including an 8 foot walk. Total daily activity was measured through an actigraphy device worn continuously on the wrist for 10 days. Composite scores for global cognitive function and 5 separate cognitive domains were derived from a battery of 19 cognitive tests. In mixed regression models adjusted for age, sex, and education, higher levels of each variable were associated with higher levels of cognitive function and less cognitive decline. In a combined model, larger life space (Estimate [Est] = 0.018, standard error [SE] = 0.006, p = 0.001), higher cognitive activity (Est = 0.017, SE = 0.008, p = 0.036), and better mobility performance (Est = 0.050, SE = 0.016, p = 0.002) were independently associated with a lower rate of cognitive decline. In summary, larger life space was associated with less cognitive decline independent of level of mobility or physical, social, or cognitive activities in community-based older adults.

008-S

REDUCED HEART RATEVARIABILITY IS ASSOCIATED WITH WORSE COGNITIVE FUNCTION IN ELDERLY MEXICAN AMERICANS.

*Adina Zeki Al Hazzouri, Mary Haan (University of California, San Francisco CA 94107)

Heart rate variability (HRV) is a subclinical measure of central autonomic function. Reduced HRV is a strong predictor of cardiovascular risk factors and events. Therefore, reduced HRV may be associated with cognitive neurodegeneration. Yet this has been relatively unexplored, particularly in minority populations. We investigated whether reduced heart rate variability was associated with worse cognitive function in elderly Mexican Americans. The Sacramento Area Latino Study on Aging (SALSA) is a prospective cohort study of 1,789 community-dwelling Mexican-Americans aged 60-101 years at baseline. SALSA includes seven annual study visits. HRV was measured in a total of 869 subjects who participated in either visit 5 or 6 and thus constituted our analytical sample. HRV was assessed using the ANS2000 which is an ECG monitor and respiration pacer measuring variability in heart rate in response to deep breathing. Cognitive function was assessed using the Modified Mini Mental State Exam (3MS), a 100-point test of global cognitive function. For ease of interpretation, we categorized HRV into quartiles (Q1 to Q4: reduced to high HRV). We fit linear regression models to estimate the associations between quartile of HRV and cognitive function (3MS). 14% of our participants reported having had a stroke, 41% had type-2 diabetes, and more than 90% had hypertension. Reduced HRV was associated with older age, lower education, having had a stroke, type-2 diabetes, hypertension, and elevated depressive symptoms. In fully-adjusted models, compared to subjects in the highest quartile of HRV, those in quartile 1 had a 4-point lower mean 3MS score ($p < 0.01$), those in quartile 2 had a 2-point lower mean 3MS score ($p = 0.04$), and those in quartile 3 had -point lower mean 3MS score ($p = 0.35$). Reduced HRV is associated with worse performance on the test of global cognitive function, above and beyond traditional cardiovascular risk factors.

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009-S

CARDIOVASCULAR RISK SCORE, COGNITIVE DECLINE AND DEMENTIA IN OLDER MEXICAN AMERICANS: THE ROLE OF GENDER AND EDUCATION. *Adina Zeki Al Hazzouri, Mary Haan (University of California, San Francisco CA 94107)

There is increasing evidence that summary scores measuring cardiovascular disease (CVD) risk are predictive of cognitive decline. Yet no prior work was conducted in low income minority populations such as Mexican Americans and has covered the whole range of CVD. In this analysis, we examine the associations of CVD risk with cognitive decline and incidence of dementia and cognitive impairment but not dementia (CIND), and the role of education as a modifier of these effects. A total 1,116 Mexican American elderly were followed annually in the Sacramento Area Latino Study on Aging. Our sex-specific CVD risk score included baseline age, SBP, total cholesterol, HDL, smoking, BMI, and diabetes and it predicted the 10-year risk of developing CVD. From adjusted linear mixed models, errors on the Modified Mini-Mental State Exam (3MSE) were annually 0.41% lower for women at the 25th percentile of CVD risk, 0.11% higher at the 50th percentile and 0.83% higher at the 75th percentile (p-value of CVD risk x time <0.01). In men, 3MSE errors were annually 1.76% lower at the 25th percentile of CVD risk, 0.96% lower at the 50th percentile and 0.12% higher at the 75th percentile (p-value of CVD risk x time < 0.01). From adjusted linear mixed models, the annual decrease in the Spanish and English Verbal Learning Test score was 0.09 points for women at the 25th percentile of CVD risk, 0.10 points at the 50th percentile, and 0.12 points at the 75th percentile (p-value of CVD risk x time = 0.02). From adjusted Cox models in women, compared to <6 years, having 12+ years of education was associated with 76% lower hazard of dementia/CIND (95%CI = 0.08,0.71) at the 25th percentile of CVD risk and with 45% lower hazard (95% CI = 0.28,1.07) at 75th percentile (p-value of CVD risk x education = 0.05). CVD risk score may provide a useful tool to identify individuals at risk for cognitive decline and dementia.

010-S

LONGITUDINAL AND RECIPROCAL RELATIONSHIPS BETWEEN DEPRESSION AND DISABILITY IN OLDER WOMEN CAREGIVERS AND NON-CAREGIVERS: RESULTS FROM CAREGIVER-SOF. *Kathy Bacon, Tim Heeren, Julie Keysor, Lisa Fredman (Boston University School of Public Health, Boston MA 02118)

Depressive symptoms and disability each increase the risk of the other condition, yet few studies have examined reciprocal associations between these conditions in a single study, or over periods longer than 3 years. Further, an estimated 48.9 million adults are caregivers, many of them elderly, but how the burden of caregiving affects such associations is unknown. Using data on 956 older women (mean [m] age = 81.5) from the Caregiver-Study of Osteoporotic Fractures, we used structural equation models to investigate relationships between depression and disability over 3 interviews spanning 1999-2006. Separate models were performed for the 611 non-caregivers (NCG) and 345 caregivers to a relative or friend (CG). We measured depression by the Center for Epidemiologic Studies-Depression Scale (CESD) and disability by a count of limitations in 7 Basic and 7 Instrumental Activities of Daily Living (ADL/IADLs). At each interview, NCGs had significantly more ADL/IADL limitations (m = 1.2 sd = 1.7) than CGs (m = 0.7 sd = 1.1), but did not differ significantly in CESD score (NCG m = 7.1 sd = 6.3, CG m = 7.8 sd = 7.0). Age-adjusted results showed reciprocal associations in that more depressive symptoms predicted greater ADL/IADL limitations, while greater limitations predicted higher CESD scores at the next interview (m interval = 2.8 years) in NCGs (standardized path coefficients range 0.07 to 0.14, p < 0.05) but not for CGs (coefficients range -0.02 to 0.03, p > 0.50). In sum, older women CGs may be less vulnerable than NCGs to the adverse impacts of depressive symptoms and ADL/IADL limitations on each other because they may be buffered by better physical condition, social interaction, and resilience related to performing caregiving activities.

011

HALOPERIDOL IN ELDERLY USERS: NOT A CAUSE OF DEATH, BUT CAUSED BY IMPENDING DEATH? *Hendrika Luijendijk, Niels de Bruin, Xander Koolman (BAVO Europoort, Rotterdam, The Netherlands)

Background and aim: Large and meticulous observational studies have reported an association between conventional antipsychotics and an increased risk of mortality in elderly users. However, meta-analyses of randomized trials have proven the safety of these drugs compared to placebo. Terminal illness may explain the conflicting findings. More than 80% of terminally ill patients experience delirium and haloperidol is the drug of preference. In addition, terminal illness predicts death. Yet, it is seldom reported in medical records, which are often used for observational studies. The aim of this study was to assess whether terminal illness has confounded the observational findings. Methods: A review of fifteen cohort studies that analysed the association between new use of conventional antipsychotics and death compared to atypical antipsychotic or no use. Patients were aged 65 or older and lived in the community or in a nursing home (n 2385 – 82012). Seven studies were restricted to patients with dementia. Data were collected retrospectively from medical files and pharmaceutical claims. We abstracted from the publications (1) patient characteristics and deaths that may point to terminal illness, and (2) methods that were used to adjust for terminal illness. Results: Sicker and older patients received conventional antipsychotics more often than new antipsychotics. The risk of dying was especially high in the first month of use, and when haloperidol was administered by injection only or in high dosages. A considerable number of patients using haloperidol died of causes without an apparent relationship to the drug's pharmacokinetics. Terminal illness was not measured in any study. Some studies adjusted for delirium, but the low rates of delirium indicated that it had been poorly identified and reported. Other studies applied instrumental variable analysis to control for confounding by unmeasured variables. However, the chosen instrument (the doctor or nursing home preference for conventional or atypical drugs) may have been influenced by terminal illness. Conclusions: Terminal illness has not been adjusted for adequately in any of the observational studies. Therefore, the association between conventional antipsychotics and increased risk of dying in the elderly cannot be causally inferred.

012-S

ASSOCIATION OF ALZHEIMER RELATED GENOTYPES WITH COGNITIVE DECLINE IN THREE CITY-DIJON STUDY. *Alexandre Vivot, Maria Glymour, Christophe Tzourio, Genevieve Chene, Carole Dufouil (Harvard School of Public Health; Department of Social and Behavorial Sciences, Boston MA 02215)

Introduction: Several genetic loci have been associated with late-onset Alzheimer Disease (LOAD), but their association with cognitive function and cognitive decline remains unclear. We sought to confirm that 5 genes known to predict LOAD also predict cognitive function and decline in a prospective cohort. Methods: Three City Study cohort (age 65 + years) participants in the Dijon site were genotyped for APOE, CR1, BIN1, CLU and PICALM polymorphisms. Respondents were assessed up to 5 times over 10 years with a neuropsychological tests battery including: Mini Mental State Examination (MMSE) for global cognition and Isaac Set Test after 30s (IST30) for verbal fluency. Mean differences at baseline and in rate of decline were estimated by mixed model with a latent process. Results: We included 4599 people with 17593 MMSE and 17581 IST30 evaluations. Median number of evaluations (MMSE and IST30) per subject was 4, Interquartilerange (IQR) = 3-5. Median value of MMSE was 28 (IQR = 26-29), median value of IST30 was 49 (IQR = 41-56). APOE e4 allele carriers had a faster decline in both MMSE (Mean difference in Z scores = -0.13, p = 002) and IST30 (-0.21, p = 0.005). Carriers of BIN1 G allele had higher baseline MMSE (0.13, p = 0.03) and a faster MMSE decline (-0.11, p = 0.02). Carriers of CR1 C allele had higher baseline IST30 (0.21, p = 0.02) and faster decline for IST30 (-0.14, p = 0.06). CLU and PICALM were not associated with baseline or rate of change on MMSE nor IST30. Conclusion: We found some evidence for an association of the top-associated SNPs in LOAD and cognitive function in elderly people, but associations were not confirmed in 2 of 5 loci. Further analyzes will be undertaken to confirm these negative results.

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013-S

DO BEHAVIORAL FACTORS PREVENT FUNCTIONAL DISABILITY AMONG COGNITIVELY IMPAIRED ADULTS? AN INVERSE PROBABILITY WEIGHTED ANALYSIS. *Pamela Rist, Benjamin Capistrant, Qiong Wu, M. Maria Glymour (Harvard School of Public Health, Boston MA 02115)

Cognitive impairment predicts losses in the ability to independently manage activities of daily living (ADLs) but does not affect everyone equally. We followed 7,350 Health and Retirement Study participants aged 65+ and without activity limitations in 1998 biennially for 12 years to identify factors that preserve independence even in the context of cognitive losses. Hypothesized modifiers included physical activity and alcohol consumption. Dementia probability score, a measure of cognitive impairment, was divided into four categories with higher categories representing increased dementia probability. Dementia categories and modifier status were assessed one wave prior to activity assessment. We tested multiplicative interaction terms between each modifier and dementia category in pooled logistic regression models using inverse probability weights to adjust for time-varying confounders and attrition. Increasing dementia category predicted increased risk of ADL limitations (odds ratio (OR) = 1.50; 95% CI: 1.39-1.62). Past wave physical activity was protective against incident ADL limitations (OR = 0.59; 95% CI: 0.42-0.83) while past wave alcohol consumption had little effect (OR = 0.93; 95% CI: 0.73, 1.18). Interaction terms between physical activity or alcohol consumption and dementia probability score were not significant on a multiplicative scale (p-values = 0.72 and 0.59, respectively). For people with lowest dementia scores, physical activity reduced the probability of incident ADL limitations by 3 percentage points (0.13 to 0.10), but for people with highest dementia scores, physical activity reduced the probability of incident ADL limitations by 7 percentage points (0.35 to 0.28). In contrast, alcohol consumption resulted in a 1 percentage point increase in the probability of incident ADL limitations for low and high dementia scores. These results suggest physical activity may reduce the risk of activity limitations after onset of cognitive impairment.

014-S

STRESSFUL EXPERIENCES, SOCIAL SUPPORT, AND GENE-SOCIAL ENVIRONMENT INTERACTION IN COGNITIVE FUNCTION: FINDINGS FROM THE WISCONSIN REGISTRY FOR ALZHEIMER'S PREVENTION (WRAP). *Megan Zuelsdorff, Corinne Engelman, Elliot Friedman, Rebecca Koscik, Erin Jonaitis, Asenath La Rue, Mark Sager (Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health, Madison WI 53726)

Objective: Cognitive aging is influenced by a complex set of variables. We examined relationships between stressful events, social support, and cognitive function in late middle-aged adults with a family history of Alzheimer's disease (AD) enrolled in the Wisconsin Registry for Alzheimer's Prevention (WRAP). Methods: WRAP participants completed neuropsychological tests and psychosocial questionnaires. Outcomes included cognitive factor scores: speed and flexibility (SF), verbal learning and memory (VLM), and working memory (WM). Key predictors included standardized index scores for stressful events and social support. Multiple regression tested for main effects of each predictor variable, adjusting for participant age, gender, education, and number of APOE ε4 alleles. In secondary analyses, measures of health and lifestyle (BMI, smoking, and partner status) were added to models and relationships were reexamined. Finally, interactions between the two psychosocial variables themselves and with number of APOE ε4 alleles were assessed. Results: Sample mean (sd) age was 56.7 (6.5) years (n = 623). Primary analyses showed relationships which were significant at the $p < .05$ level between SF and stress (beta = -.117) and between SF and social support (beta = .106) but not between VLM or WM and stress or support. Secondary analyses indicated that these relationships remained significant after accounting for health and lifestyle factors. In interaction models, a significant, negative interaction between social support and number of APOE ε4 alleles was seen (beta = -.118). Conclusion: As the population ages, the need to identify modifiable risk factors for cognitive decline intensifies. Findings suggest that psychosocial factors may influence cognitive function in populations of intact but at-risk individuals, and that this influence varies according by cognitive domain as well as by presence of specific genetic risk factors.

015

FACTORS ASSOCIATED WITH PARENTAL ACCEPTABILITY OF HUMAN PAPILLOMA VIRUS VACCINATION IN SOUTHERN INDIA. *Purnima Madhivanan, Tan Li, Ahmed Albatineh, Soumyadeep Mukherjee, Vijaya Srinivas, Anjali Arun, Karl Krupp (Robert Stempel College of Public Health, Florida International University, Miami FL 33199)

Background: It has been estimated that widespread uptake of Human Papilloma Virus (HPV) vaccine by adolescent girls could reduce incidence and mortality of cervical cancer by approximately two-thirds. This study explores correlates of parental HPV vaccine acceptability in Mysore, India. Methods: Between August and December of 2011, stratified, multi-stage random sampling was used to recruit students in schools located in Urban Mysore. Questionnaires were sent home with 800 adolescent girls attending 10 schools to be completed by a parent. Logistic regression was used to assess factors associated with parental acceptability of HPV vaccine. Results: 797 completed surveys were received with 72% respondents accepting HPV vaccine for their daughters. Vaccine acceptance was higher among participants who had experienced cancer in their family(Odds Ratio [OR]: 1.69, 95% Confidence Interval [CI]: 1.07-2.65), or perceived that their family doctor (5.04; 3.27-7.76) or spouse (5.01; 3.20-7.87) would approve. Muslim parents (0.54; 0.37-0.80), parents having concerns about vaccinations in general (0.38; 0.25-0.57), vaccine side-effects (0.65; 0.45-0.94), vaccine safety (0.64; 0.42-0.97) or the possibility that their daughter might become sexually active (0.71; 0.28-0.76) had lower odds of accepting HPV vaccination. Conclusion: The majority of parents of school-going adolescent girls in Mysore found HPV immunization acceptable. Further research is needed to understand the issues associated with HPV vaccination in different religious groups in India.

016

ADULT STATURE AND RISK OF CANCER AT DIFFERENT ANATOMIC SITES IN A COHORT OF POSTMENOPAUSAL WOMEN. *Geoffrey Kabat, Moonseong Heo, Dean Hosgood, Victor Kamensky, Jennifer Bea, Dorothy Lane, Matthew Anderson, Jean Wactawski-Wende, Jo Ann Manson, Thomas Rohan, Lifang Hou (Albert Einstein College of Medicine, Bronx NY 10461)

A small number of prospective studies in Western and Asian populations have indicated that height may be an independent risk factor for various cancers. However, there is some inconsistency regarding which sites are associated with height. Furthermore, few studies have explored potential confounding and effect modification of the association. We examined the association between height measured at baseline in 144,701 women enrolled in the Women's Health Initiative and risk of all cancers and of cancer at 19 specific sites. Over a median follow-up of 12.0 years, 20,928 incident cancers were identified. We used Cox proportional hazards models to estimate hazard ratios (HR) and 95% confidence intervals (95% CI) per 10 cm increase in height, with adjustment for established risk factors. Height was significantly positively associated with risk of all cancers (HR 1.08, 95% CI 1.05-1.10), as well as with cancers of the colorectum, thyroid, melanoma, and multiple myeloma (range of HRs: 1.09 for colorectal cancer to 1.32 for thyroid cancer). In addition, other sites showed borderline positive associations: colon, rectum, breast, ovary, cervix, brain, and non-Hodgkin's lymphoma. These associations were generally insensitive to adjustment for confounders and showed little variation by level of other variables. Of 19 cancer sites, none showed a significant inverse association with height. The present study confirms the association of height with risk of all cancers and a substantial number of cancer sites. While adult height is influenced by both genetics and early life exposures, further studies are needed to clarify possible mechanisms underlying the associations of height with specific cancers.

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017-S

INCIDENCE PATTERNS AND TRENDS OF GONADAL AND EXTRAGONADAL GERM CELL TUMORS IN GERMANY, 1998-2008.

*Carsten Rusner, Britton Trabert, Andreas Stang, on behalf of the Network of German Cancer Registries (GEKID) (Institute of Clinical Epidemiology, Medical Faculty, Martin-Luther-University of Halle-Wittenberg, Halle (Saale) Germany)

Gonadal (GGCT) and extragonal germ cell tumors [GCT (EGCT)] are thought to originate from primordial germ cells. In contrast to well reported population-based data of GGCTs in males, analyses of GGCTs in females and EGCTs in both sexes remain limited. The aim of this study was to provide updated incidence rates of GGCTs and EGCTs with special interest in detailed analysis of extragonadal sites. In a pooling project of nine population-based cancer registries in Germany of the years 1998-2008, 16,883 GCTs and their topographical sites were identified using morphology and topography codes of the International Classification of Disease for Oncology for those aged 15 years and older. We estimated age-specific and age-standardized incidence rates. Among males, the incidence of testicular GCTs increased while the incidence of EGCT remained stable over time. Among women, the incidence of ovarian GCTs remained stable while the incidence of EGCTs declined over time. The most frequent extragonadal sites were mediastinum and brain among males, and placenta and uterus among females. The age-specific incidence patterns of testicular GCTs had a steep increase starting at ages 15 up to 34. In contrast, rates of ovarian GCTs decreased in these ages. Among EGCTs, mediastinum in males and placenta in females showed similar patterns as testicular GCTs, whereas GCTs of brain and pineal gland in males fell at ages 15 up to 29. In conclusion, our results underline different incidence patterns and trends in GGCTs and EGCTs. The differences suggest that GGCTs and EGCTs may have different etiologies.

018-S

LIFETIME BODY SIZE AND PROSTATE CANCER RISK IN A POPULATION-BASED CASE-CONTROL STUDY IN SWEDEN.

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Background: Body size appears to be associated with prostate cancer risk, but the relationship is complex and may vary between different periods in life and disease subtypes. We investigated if body size in childhood and adulthood is related to total, high-risk and low-risk prostate cancer. Methods: We used data on 1499 incident cases and 1118 population controls in the Cancer of the Prostate in Sweden study. A 5-size pictogram assessed body figure at age 10. Age-specific and mean adult BMI was calculated based on self-reported height and recalled weight at ages 20-70 years. Weight change during adulthood was examined using beta coefficients from linear regression models of BMI against age. Odds ratios (OR) and 95% confidence intervals (CI) were estimated by unconditional logistic regression. Results: Being thin at age 10 was inversely associated with total and low-risk disease compared to being normal weight (multivariate ORs 0.80, 95% CI 0.66-0.99, and 0.74, 95% CI 0.57-0.95). Men in the three highest quartiles of height had statistically significantly higher risks of all disease subtypes compared to the lowest quartile (ORs ranging 1.28-1.53). A mean adult BMI of 25- < 30 was protective against low-risk disease compared to BMI <25 (OR 0.73, 95% CI 0.57-0.94). Comparing the second tertile of the beta coefficient (increase 0.05-0.12 BMI units/year) to the first tertile, we observed a 30% increased risk of all disease subtypes. Conclusions: Our results suggest being thin in childhood or overweight in adulthood may protect against low-risk disease; tall height and modest weight gain in adulthood may increase the risk of overall disease. However, these results should be interpreted with caution as no clear dose response was observed.

019-S

ACRYLAMIDE HEMOGLOBIN ADDUCTS LEVELS AND OVARIAN CANCER RISK IN THE NURSES' HEALTH STUDY.

*Jing Xie, Kathryn Terry, Elizabeth Poole, Kathryn Wilson, Bernard Rosner, Walter Willet, Hubert Vesper, Shelley Tworoger (Harvard School of Public Health, Boston MA 02115)

Background: Acrylamide is a probable human carcinogen formed during cooking of starchy foods. Two large prospective cohort studies of dietary acrylamide intake and ovarian cancer risk observed a positive association, although two other studies reported no association. Methods: We measured acrylamide exposure using red blood cell acrylamide and glycidamide hemoglobin adducts among women in two large prospective cohorts: the Nurses' Health Study and Nurses' Health Study II. Between blood collection and 2010, we identified 263 incident cases of epithelial ovarian cancer, matching two controls per case. We used logistic regression models to examine the association between acrylamide exposure and ovarian cancer risk, adjusting for matching factors, family history of ovarian cancer, tubal ligation, oral contraceptive use, body mass index (BMI), parity, alcohol intake, smoking, physical activity, and caffeine intake. Results: The multivariate-adjusted relative risk (RR) of ovarian cancer comparing the highest versus lowest tertile of total acrylamide adducts was 0.79 (95% CI: 0.50-1.24, P trend = 0.08). The comparable RR of ovarian cancer among nonsmokers at blood draw was 0.85 (95% CI: 0.57-1.27, P trend =0.14). The association did not differ by tumor histology (serous invasive versus not), P for heterogeneity = 0.41. Individual adduct types (acrylamide or glycidamide) were not associated with risk. Conclusions: We observed no evidence that acrylamide exposure as measured by adducts to hemoglobin is associated with an increased risk of ovarian cancer. Impact: Our finding indicates that acrylamide intake may not increase risk of ovarian cancer.

020-S

GASTROINTESTINAL STROMAL TUMORS: LINKING SINGLE NUCLEOTIDE POLYMORPHISMS AND SOMATIC MUTATIONS.

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Gastrointestinal stromal tumors, or GISTs, are a rare form of soft tissue sarcoma that develop from mesenchymal cells with acquired gain-in-function mutations in KIT or PDGFRA oncogenes. These somatic mutations have been well-characterized, but little is known about inherited genetic risk factors of GIST. Given previous evidence that certain susceptibility loci and carcinogens are associated with characteristic mutations in other cancers, these signature KIT or PDGFRA tumor mutations may be fundamental to understanding GIST etiology. We examined the association between 522 candidate single nucleotide polymorphisms (SNPs) and 7 KIT or PDGFRA tumor mutations types. Candidate pathways included dioxin response, toxin metabolism, matrix metalloproteinase production, and immune and inflammatory response. Using logistic regression, we estimated odds ratios (ORs) and 95% confidence intervals (CI) for the association between each candidate SNP and tumor mutation type in 279 individuals from a clinical trial of adjuvant imatinib mesylate. We also used sequence kernel association tests (SKAT) to look for pathway-level associations. After controlling for a false discovery rate of 25%, one SNP, rs1716 on ITGAE, was significantly associated with KIT exon 11 non-codon 557 deletions (OR = 2.9, 95% CI: 1.7, 4.8, p = 6 × 10-5). Other noteworthy associations included rs3024498 (IL10) and rs1050783 (F13A1) with PDGFRA mutations (OR = 0.3, 95% CI: 0.2,0.6 and OR = 0.3, 95% CI: 0.2,0.6, respectively), rs2071888 (TAPBP) with wildtype tumors (OR = 0.4, 95% CI: 0.2, 0.7), and several matrix metalloproteinase SNPs with KIT exon 11 codon 557 deletions. Several pathways were strongly associated with somatic mutations in PDGFRA, including defense response (p = 0.005) and negative regulation of immune response (p = 0.01). This exploratory analysis offers novel insights into GIST etiology and provides a starting point for future studies of genetic and environmental risk factors for the disease.

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021

ANATOMIC SUBSITE OF PRIMARY COLORECTAL CANCER AND SUBSEQUENT RISK AND DISTRIBUTION OF SECOND CANCERS.

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Individuals with a history of colorectal cancer have an increased risk of subsequent cancer. We used data from 12 Surveillance Epidemiology and End Results (SEER) cancer registries to assess whether this increased risk of second cancers differed by anatomic subsite of the index colorectal cancer. Index cases included individuals diagnosed with first primary colorectal cancer between 1992-2009. Using SEER*Stat software, we calculated standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) comparing the incidence of second cancers in these index cases to cancer incidence rates in the general population. SIRs were calculated for cancers at anatomic sites within and outside the colorectum in analyses stratified by index colorectal cancer subsite. Cancer incidence rates were significantly higher in those with prior colorectal cancer than in the general population (SIR = 1.15, 95% CI: 1.13-1.16). Cases with an index colorectal cancer located between the transverse and descending colon experienced the greatest increased risk of second cancer overall (SIR = 1.29 to 1.33) and second colorectal cancer in particular (SIR = 2.53 to 3.35). Incidence of small intestinal cancer was significantly elevated regardless of index colorectal cancer subsite (SIR = 4.31, 95% CI: 3.70-4.77). Incidence of endometrial cancer was elevated in those with index proximal colon cancer (SIR = 1.37 to 1.79). These findings suggest that risk of second cancer after colorectal cancer differs by anatomic site of the index colorectal cancer, and is particularly pronounced for those with index cancer in the transverse to descending colon. Second cancers were most likely to occur in embryologically-related tissues, which may share similar susceptibility to aberrant molecular changes induced by shared exposures.

022

INCREASING INCIDENCE OF THYROID CANCER IN MINHANG DISTRICT, SHANGHAI, IN 2002-2010.

*Hong Fang, Yanping Zhao, Huilin Xu, Yujie Yan, Xiuhong Tian, Na Wang, Lingfang Feng, Yue Chen, Qingwu Jiang (Shanghai Minhang Center for Disease Control and Prevention, Shanghai China)

A great attention has been paid to an increase in the incidence of thyroid cancer in several countries. The authors investigated the changing pattern of thyroid cancer incidence in Minhang District, Shanghai, using data derived from the Shanghai Cancer Registry for the period from 2002 to 2010. Crude and age-standardized incidence rates were calculated for men and women separately. Percent change (PC %) and annual percent change (APC %) were estimated for the incidence rates of thyroid cancer. In total, there were 901 thyroid cancer cases for the study period. The age-standardized incidence rate of thyroid cancer in Minhang increased from 4.11 per 100 000 in 2002 to 15.05 per 100 000 in 2010, a 3.66-fold increase. PC % and APC % were 163.67% and 17.35% for men and 264.12% and 21.41% for women, respectively. In 2002, thyroid cancer accounted for only 1.41% of all cancer cases, while in 2010 it was 5.51%. Thyroid cancer was the third most frequent cancer type in women and 11th in men in 2010. The authors concluded that the incidence of thyroid cancer had been increasing sharply in Minhang. Reasons for this increase are not known. Future studies will focus on changes in potential pathogenic risk factors and/or diagnostic technologies.

023-S

INCIDENCE OF PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA FROM 1992 THROUGH 2007: A SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS ANALYSIS.

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Background: Primary central nervous system lymphoma (PCNSL) is an extranodal non-Hodgkin lymphoma arising in the craniospinal axis. Incidence rates of PCNSL in the U.S. have increased since the early 1970s, attributed in part to the HIV epidemic, as AIDS is a risk factor for PCNSL and PCNSL is an AIDS-defining illness. It is unclear whether incidence rate trends are homogeneous across gender, age, year of diagnosis, and race. The objective of this study was to characterize gender- and race-specific, subsite-specific, and overall age and temporal patterns of PCNSL incidence in the U.S. Methods: Incidence data for PCNSL from 1992 through 2007 were derived from SEER-13. Age-adjusted incidence rates were calculated overall and by subsite according to sex, race, age, and calendar period using SEER*Stat. Rate ratios with corresponding 95% confidence intervals were used for making comparisons. Results: Primary CNS lymphoma remains primarily a disease associated with age, based on our findings. However, older Blacks experience lower rates than their White and Asian counterparts and in recent years, Blacks overall have slightly lower incidence rates. Urban registries continue to report higher incidence rates than state-wide counterparts. PCNSL occurs most often in the brain, followed by eye, then spinal cord and other sites. Period analysis of incidence rates and age distributions shows that the biphasic incidence trends and bimodal age distributions for males were transient, diminishing in the late-1990s through 2001 and remaining near constant thereafter. Conclusions: Incidence rates for PCNSL increased progressively through the 1980s, leveled off in the mid- to late-1990s, decreased, and are now only slightly higher compared with recent past years. Rate trends are different by gender, age, and race, suggesting multiple disease etiologies. Further investigation into the recent lower incidence rates among Blacks may yield novel prevention strategies.

024-S

THE HEALTHY EATING INDEX-2005 AND RISK OF PANCREATIC CANCER IN THE NIH-AARP DIET AND HEALTH STUDY.

*Hannah Arem, Jill Reedy, Joshua Sampson, Li Jiao, Albert Hollenbeck, Harvey Risch, Susan Mayne, Rachael Stolzenberg-Solomon (Yale University, New Haven, CT 06520)

Background: Dietary pattern analyses characterizing combinations of food intakes offer conceptual and statistical advantages over food and nutrient based analyses of disease risk. However, few studies have examined dietary patterns and pancreatic cancer risk and none focused on the 2005 Dietary Guidelines for Americans. We used the Healthy Eating Index-2005 (HEI-2005) to estimate the association between meeting those dietary guidelines and pancreatic cancer risk. Methods: Using responses to 1995-1996 food-frequency questionnaires, we calculated the HEI-2005 score for 537,218 men and women in the National Institutes of Health-AARP Diet and Health Study. We followed these individuals through 12/31/2006 to identify exocrine pancreatic cancer cases. We used Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% confidence interval (CIs) for risk of pancreatic cancer according to HEI-2005 quintiles and explored effect modification by known risk factors. Results: We identified 2,383 incident, exocrine pancreatic cancer cases (median 10.5 years follow-up). Comparing participants who met the most dietary guidelines (Quintile 5) to those who met the fewest guidelines (Quintile 1), we observed a reduced risk of pancreatic cancer (HR = 0.85, 95% CI 0.74-0.97). Among men there was an interaction by body mass index (BMI)(p-interaction = 0.028), with a HR = 0.72 (95% CI 0.59-0.88) comparing Q5 versus Q1 in overweight/obese men (BMI $\geq$ 25 kg/m2) but no association among normal weight men. Conclusions: Our findings support the hypothesis that consuming a high-quality diet, as scored by HEI-2005, may reduce the risk of pancreatic cancer.

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025

TRENDS IN THE OCCURRENCE OF HIGH-GRADE ANAL INTRAEPITHELIAL NEOPLASIA IN SAN FRANCISCO: 2000-2009.

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Although screening of HIV-positive individuals for anal intraepithelial neoplasia (AIN, the anal cancer precursor) has been practiced by many HIV healthcare providers in San Francisco since the early 1990s, no prior study has focused on evaluating AIN trends. Such an evaluation would inform clinicians, pathologists, and agencies planning prevention activities. The authors selected cases of high-grade AIN 3 and invasive anal cancer (2000-2009) from the San Francisco/Oakland Surveillance, Epidemiology, and End Results (SEER) population-based cancer registry. Age-standardized AIN 3 and invasive anal cancer rates were calculated overall and by demographic characteristics (sex, race, and age group). Log-linear regression calculated annual percent change in rates during 2000-2009, and rate ratios (RRs) and 95% confidence intervals (CIs) evaluated differences in rates during 2000-2004 and 2005-2009. Most AIN 3 cases occurred among men (87.27%, 1152/1320) during 2000-2009. AIN 3 rates during the corresponding period increased by 11.59%/year ($P < 0.05$) among men and were stable among women. Comparing rates among men during 2000-2004 to those in 2005-2009, the largest increases were among those aged 45-64 years (RR, 2.08, 95% CI, 1.73-2.51) and among blacks (RR, 3.49, 95% CI, 2.14-5.84). During the same time period invasive anal cancer rates were stable among men and women. In summary, rates of AIN 3 increased in San Francisco during 2000-2009, in conjunction with an anal cytology screening program for high risk invidivuals, while rates of invasive anal cancer were unchanged. Continued surveillance is necessary to evaluate the impact of screening as well as human papillomavirus (HPV) vaccination coverage on the prevention of HPV-related AIN and anal cancer.

026

A STUDY OF THYROID CANCER INCIDENCE IN CLOSE PROXIMITY TO SIX NUCLEAR POWER FACILITIES IN THE STATE OF NEW YORK: A DESCRIPTIVE ANALYSIS.

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Background: Several epidemiological studies have investigated the cancer risks associated with nuclear accidents while few have published on the effects of living in close proximity to a normally functioning nuclear facility. The purpose of this paper is to evaluate whether an association exists between chronic low level radiation exposure from nuclear facilities and future increased risk of thyroid cancer. Methods: Information on thyroid cancer incidence in New York State was obtained from the Department of Health's Metrix website for 2005-2009. Census data provided latitude and longitude coordinates for the central location of each geographic region in NYS. Distance in kilometers from each geographic area to each of the six nuclear facilities in New York State was calculated with SAS v9.2 (SAS Institute, Cary, NC). Observed and expected thyroid cancer counts were compared for three regions of distance from nuclear facilities. The incidence rate ratios and 95% confidence intervals for thyroid cancer for individuals living within 5 kilometers, 16 kilometers, and 30 kilometers of any of the six nuclear facilities was 1.01 (.73-1.35), .84 (.75-.94), and 1.04 (.99-1.10) for the 5 kilometers, 16 kilometers, and 30 kilometers cohorts respectively while the incidence rate ratop for thyroid cancer near the four major facilities was 1.00 (.49-1.35), 1.01(.86-1.18), and 1.07 (1.00-1.14). Conclusions: This work is among the first to report on data recently compiled by the New York State Cancer Registry and made available to the public. In this study, no association was found between living in close proximity of nuclear facilities and increased thyroid cancer incidence. The work and analysis done here can be used to facilitate further research on the topic of cancer incidence in close proximity to nuclear power facilities.

027

CANCER RISKS IN CHILDREN WITH CONGENITAL MALFORMATIONS IN THE NERVOUS SYSTEM.

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Aim: We estimated the overall and organ-specific cancer risk at different ages for children with a congenital malformation (CM) in the nervous system. Methods: We identified 1,711,335 live born singletons in Denmark 1 January 1977 and 31 December 2007. We followed children from the date of birth until the time of cancer diagnosing, death, emigration, or 31 December 2007. Children entered in a cohort if they were diagnosed with a CM in the nervous system. Information on CMs in children was obtained from the Danish National Hospital Register. Information on cancer was obtained from the Danish Cancer Registry. We applied Cox proportional hazards regression model to estimate the hazard ratio (HR) for cancer. Results: Among 1,711,335 children, 4,844 (0.28%) were diagnosed with a CM in the nervous system and 4,149 (0.24%) were diagnosed with cancer during up to 30 years follow up including 48 children with a CM in the nervous system. Children with a CM in the nervous system had 4.5 fold (HR = 4.48, 95%CI: 3.37-5.96) overall risk of cancer. The cancer risk was extremely high in the first month of life (HR = 125.81, 95%CI: 37.41-423.13). The highest cancer risk were found in the mesothelial and soft tissue (HR = 18.23, 95%CI: 9.27-35.85) and in the central nervous system (HR = 11.88, 95%CI: 7.09-19.93). The overall cancer risks were higher for children with spina bifida or hydrocephalus. Conclusions: Children who have a CM in the nervous system had an increased risk of cancer.

028-S

ADOLESCENT CAROTENOID INTAKE IN RELATION TO BENIGN BREAST DISEASE.

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Carotenoids may reduce risk of benign breast disease (BBD), an independent risk factor for breast cancer, through antioxidative or antiproliferative mechanisms. Exposure to carotenoids may be most important during adolescence when breast tissue is still developing. We sought to examine adolescent intake of carotenoids and vitamin A in relation to BBD. In 6610 adolescent girls in the prospective Growing Up Today Study cohort, we assessed mean intake of total carotenoids, alpha carotene, beta carotene, beta cryptoxanthin, lycopene, lutein and zeaxanthin, and vitamin A using annual food frequency questionnaires in 1996, 1997, 1998 and 2001. Girls reported biopsy-confirmed BBD on questionnaires in 2005, 2007, and 2010 (n = 123). We conducted logistic regression adjusted for age, family history of breast cancer or BBD, height, age at menarche, parity, alcohol intake, total energy intake, body mass index, and physical activity. Mean (standard deviation) age at baseline in 1996 was 12.0 (1.6) years. In general, carotenoids and vitamin A were not associated with BBD. However, there were suggestive inverse associations of alpha carotene and beta carotene with BBD; comparing the highest to lowest quintile of intake, the odds ratios (OR) and 95% confidence intervals (95% CI) were 0.60 (0.33, 1.08; p-trend = 0.07) for alpha carotene and 0.64 (0.36, 1.16; p-trend = 0.10) for beta carotene. Lycopene was borderline positively associated with BBD, but the association was not monotonic and seemed to be driven by the top quintile [quintile 5 vs. quintile 1 OR (95% CI): 1.61 (0.94, 2.73; p-trend = 0.03)]. Adolescent alpha and beta carotene intake may be associated with reduced BBD risk and should be studied further. However, vitamin A and the other carotenoids were not associated with BBD risk in this prospective cohort.

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029-S

PLASMA ADIPONECTIN AND SOLUBLE LEPTIN RECEPTOR AND RISK OF COLORECTAL CANCER: A PROSPECTIVE STUDY.

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Adipokines are adipocyte-secreted hormones that may mediate the etiologic link between obesity and colorectal cancer (CRC); however, the evidence from large prospective studies is limited. We prospectively evaluated the association of plasma adiponectin and soluble leptin receptor (sOB-R) with colorectal cancer (CRC) risk within the Nurses' Health Study (1990-2008) and the Health Professionals Follow-up Study (1994-2008) among 616 incident CRC cases and 1,205 controls selected using risk-set sampling and matched on age and date of blood draw. We used logistic regression to estimate relative risks (RRs) and confidence intervals (CIs). Plasma adiponectin was significantly associated with reduced risk of CRC among men, but not among women, after adjustment for matching factors and potential risk factors for CRC, including family history, endoscopy screening, history of polyp, physical activity, multivitamin and aspirin use, smoking, alcohol consumption, plasma 25-hydroxyvitamin D, and dietary score. Compared to men in the lowest quartile of adiponectin, men in the highest quartile had a multivariate RR for CRC of 0.55 (95% CI: 0.35, 0.86; *P* for trend = 0.02). The corresponding RR in women was 0.96 (95% CI: 0.67, 1.39; *P* for trend = 0.74). Plasma sOB-R was not associated with overall CRC risk in either men (Quartile 4 vs. Quartile 1: multivariate RR = 0.61; 95% CI: 0.40, 0.93; *P* for trend = 0.09) or women (Quartile 4 vs. Quartile 1: multivariate RR = 1.23; 95% CI: 0.77, 1.97; *P* for trend = 0.81). A significant heterogeneity was noted in the association between sOB-R and CRC by subsite in women (*P* for heterogeneity = 0.04); sOB-R was significantly associated with increased risk of rectal cancer but not colon cancer. We did not find any significant interaction between plasma adiponectin and sOB-R on risk of CRC (*P* for interaction = 0.80 in women and 0.14 in men). In conclusion, these findings support a role for adiponectin in colorectal carcinogenesis in men. Further studies are warranted to confirm these associations and elucidate potential underlying mechanisms.

030-S

MODE OF DELIVERY AND ADIPOSITY: HONG KONG'S "CHILDREN OF 1997" BIRTH COHORT.

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Background: Both cesarean section rates and the prevalence of childhood obesity have increased in the past two or three decades worldwide. Infants delivered by caesarean section have different gut microbiota, which might affect the subsequent development of obesity. Evidence concerning the association of mode of delivery with obesity is sparse and inconsistent. We examined whether mode of delivery was associated with childhood obesity in a developed non-Western context. Methods: We used generalized estimating equations to estimate the adjusted association of mode of delivery (vaginal or cesarean) with body mass index (BMI) z-score and overweight (including obesity) from 3 months to 13 years, in 7809 term birth (94% follow-up) from a population-representative Chinese birth cohort, "Children of 1997". We used multiple imputation for missing exposure and confounders. Results: The cesarean section rate (26%) was higher for children born in private hospitals, with lower gestational age, lower birth order, higher maternal age, higher maternal BMI and higher family socio-economic position (SEP). Cesarean section was not associated with BMI z-score from 3 months to 13 years (mean difference 0.03, 95% confidence interval (CI) -0.03 to 0.09) or overweight from 3 years to 13 years (odds ratio 0.97, 95% CI 0.76 to 1.24) after adjusting for infant and maternal characteristics and family SEP. Conclusion: Cesarean section was not associated with BMI or overweight in a developed non-Western setting. Surveillance of other possible health consequences of cesarean section is required given the increasing rates of cesarean section.

031-S

PHARMACOLOGIC SEX HORMONES IN EARLY PREGNANCY AND OFFSPRING OBESITY.

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Perinatal exposure to estrogenic agents, including pharmacologic sex hormones, increases adiposity in offspring in some experimental animal models. No epidemiologic studies have assessed the association between oral contraceptive (OC) use in pregnancy and offspring adiposity. One human study of in utero diethylstilbestrol (DES) exposure and subsequent adult Body Mass Index (BMI) showed no association. We assessed the association between exposure to either DES or OC in early pregnancy and offspring obesity using data from the Collaborative Perinatal Project (1959-1974), a multicenter prospective study of pregnant women and their offspring, representing approximately 55,000 births. We estimated the odds of obesity among 35,426 children with height and weight data at 7 years of age. Obesity status was ascertained by applying the Centers for Disease Control sex- and age-specific cutpoints for the 95th percentile of BMI. BMI was calculated from height and weight as measured by study personnel. Four percent (n = 1,546) of children were obese. Exposure to an OC in the first 4 months of pregnancy was self-reported by 196 (0.5%) women and to DES by 102 (0.3%) women. We estimated robust standard errors to account for sibling clusters and adjusted for possible confounding by center, race, maternal prepregnancy BMI and smoking. OC use was weakly associated with offspring obesity (adjusted Odds Ratio (aOR): 1.38, 95% Confidence Interval (CI): 0.74, 2.56). For DES, the aOR was 1.98, 95% CI: 1.06, 3.71. We found no associations with BMI 85-95th percentile or BMI as a continuous variable. Pharmacologic sex hormone use in early pregnancy may be associated with childhood obesity. A larger study is needed to estimate the association with greater precision and with contemporary, lower-dose OC formulations.

032-S

RELATIONSHIP BETWEEN BREASTFEEDING DURATION AND WAIST-HEIGHT RATIO IN ADULTHOOD.

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Introduction: The obesity epidemic has grown into one of the most pressing public health issues facing global populations. The primary causes of the epidemic are an increasingly sedentary lifestyle and low quality diet. However, evidence suggests there are other exposures that make some more prone to becoming overweight. The current study investigated the duration one was breastfed as a possible factor. While the majority of studies involving breastfeeding have used an adolescent population, the current study attempted to establish if the relationship between breastfeeding and weight status persists into adulthood. Methods: The study sample consisted of 12,615 individuals that were part of the Add Health study. Multiple regression analysis was performed to establish if there was a relationship between the primary outcome variable, waist-height ratio (WtH), and the primary predictor variable, duration of breastfeeding (BD). In addition, behavioral and environmental risk scores were derived and included in the model as controls. Results: BD of 3-9 and >9 months were inversely related with WtH in adulthood. BD of 3-9 months was associated with a decrease in WtH of 0.015 ($p < 0.001$). BD of >9 months was associated with a decrease in WtH of 0.016 ($p < 0.001$). Conclusions: BD was related to adult WtH. This relationship existed even with inclusions of behavioral and environmental controls. Further research is warranted into the potential mechanism by which breastfeeding may be impacting adult weight status. In addition, the current study suggests that proper prenatal and perinatal nutrition along with breastfeeding could function as early interventions in the prevention of obesity from developing in individuals.

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033-S

META-ANALYSIS OF THE ASSOCIATION BETWEEN BODY MASS INDEX AND HEALTH-RELATED QUALITY OF LIFE AMONG ADULTS, ASSESSED BY THE SF-36. *Zia Ul Haq, Daniel F Mackay, Elisabeth Fenwick, Jill P Pell (Institute for Health and Wellbeing, University of Glasgow, Glasgow Scotland UK)

Background: Obesity is associated with impaired overall quality of life but individual studies suggest the relationship may differ for mental and physical quality of life. Study design: We undertook a systematic review using Medline, Embase, PsycINFO and ISI Web of Knowledge, and performed random effects meta-analysis. Studies were included in the meta-analysis if they were conducted on adults; defined as ≥16 years and if reported the overall physical and mental component score of the SF-36, and or both. Heterogeneity was assessed using I^2 statistics and publication and small study biases using funnel plots and Eggers test. Between-study heterogeneity was explored using meta-regression. Results: Eight eligible studies provided 42 estimates of effect size, based on 43,086 study participants. Adults with higher than normal BMI had significantly reduced physical quality of life with a clear dose relationship across all categories. Among morbidly obese adults, the score was reduced by 9.72 points (95% Confidence Interval 7.24, 12.20, $p < 0.001$). Mental quality of life was also significantly reduced among morbidly obese adults (-1.75, 95% Confidence Interval -3.33, -0.16, $p = 0.031$), but was not significantly different among obese individuals, and was significantly increased among overweight adults (0.42, 95% Confidence Interval 0.17, 0.67, $p = 0.001$). Heterogeneity was high in some categories, but there was no significant publication or small study bias. Conclusion: Different patterns were observed for physical and mental quality of life, but both were impaired in obese individuals. Interventions are required to address the increasing prevalence of obesity.

034-S

ASSOCIATION BETWEEN BODY MASS INDEX AND MENTAL HEALTH AMONG SCOTTISH ADULT POPULATION: A CROSS-SECTIONAL STUDY OF 37,272 PARTICIPANTS. *Zia Ul Haq, Daniel F Mackay, Elisabeth Fenwick, Jill P Pell (Institute of Health & Wellbeing, University of Glasgow, Glasgow Scotland UK)

Importance: The prevalence of overweight and obesity are increasing. Understanding the impact on health and wellbeing and how this varies will inform interventions and how they are targeted. Objective: To investigate the relationship between body mass index (BMI) and mental health, and whether it varies by sex and medical comorbidity. Design, Setting, and Participants: We undertook a cross-sectional study of a representative sample of the Scottish adult (≥16 years) population. The Scottish Health Survey provided data on mental health, measured by the General Health Questionnaire (GHQ), BMI, demographic and lifestyle information, and medical comorbidity. Univariate and multivariate logistic regression models were applied. Main Outcome Measure: Good (GHQ score <4) versus poor (GHQ score ≥4) mental health. Results: Of the 37,272 participants, 5,739 (15.4%) had poor mental health. Overall, overweight participants had better mental health than the normal-weight group (adjusted OR 0.90, 95% CI 0.84, 0.96, $p = 0.003$), and individuals who were underweight, class II or class III obese had poorer mental health (class III obese group: adjusted OR 1.21, 95% CI 1.01, 1.44, $p = 0.042$). There was a significant interaction with sex ($p = 0.013$) but not comorbidity. Being overweight was associated with significantly better mental health in men only. In contrast being underweight and classes II and III obese was associated with significantly poorer mental health in women only. Conclusion: Abnormally high and low BMI have a deleterious effect on mental health in women but not men, and overweight women do not report the increased mental health reported by men.

035

HIGH RISK OF HYPERLIPIDEMIA AND OBESITY AS A PREDICTOR IN RURAL CHINESE ADULTS: BASELINE DATA FROM THE YUHUAN RURAL HEALTH COHORT STUDY. *Chaowei Fu, Meifang Su, Xuhua Ying, Yue Chen, Songtao Li, Qingwu Jiang (Fudan University, Shanghai China)

Objective: To investigate the risk of hyperlipidemia and its association with obesity in rural adults in China. Method We conducted an analysis based on baseline data of the Yuhuan Rural Health Cohort Study. The study included all rural communities of Yuhuan County, Zhejiang Province, China. A total of 125,479 subjects aged 35 years or above participated in this study with a response rate of 71%. The current analysis included 118,571 who had blood lipid tests. Hyperlipidemia (HL) was defined as blood triglyceride ≥1.70mmol/l and/or total cholesterols ≥5.17mmol/l. Body mass index (BMI, kg/m2) was used to group subjects into three categories: obesity (≥30.0), overweight (25.0-29.9) and normal weight (<25.0). Multinomial logistic regression model was used to examine the association between obesity and hyperlipidemia, and crude and adjusted odds ratios (aORs) and 95% confidential intervals (CI) were calculated. Result: Mean BMI was 23.7 ± 3.1 for men and 23.8 ± 3.5 for women. Blood triglyceride and total cholesterols were1.59 ± 5.87mmol/l and 4.94 ± 1.50mmol/l, respectively. The prevalence was 38.4% for hypercholesterolemia (HC), 24.2% for hypertriglyceridemia (HT), 13.3% for HC and HT combined (HC + HT), and 49.3% for HL, respectively. Multinomial logistic regression analysis showed that obesity was significantly associated with HC only (aOR: 1.28, 95% CI: 1.24-1.32), HT only (3.65, 3.34-3.99), and HC + HT (4.46, 4.11-4.83) after adjustment for age, gender, education, occupation, smoking and exercise. Overweight was also significantly associated with increased risks of HC only, HT only and HC + HT. Conclusion: Hyperlipidemia was common in rural adults. Excessive body weight was an important predictor even in this population with relatively low body weight. Keywords: Hyperlipidemia, Obesity, Community, Adults, Rural.

036

FATTY LIVER'S ASSOCIATION WITH ADIPOSITY INDICATORS AMONG US ADULTS. *Henry Kahn, Yiling Cheng (Centers for Disease Control and Prevention, Atlanta GA 30341)

Fatty liver (FL)–a common condition contributing to diabetes (type 2 & gestational), atherosclerosis, liver cancer, and cirrhosis–may go unrecognized in primary care. Ultrasonograms from the 3rd National Health & Nutrition Examination Survey were recently reviewed to yield 12,915 liver assessments that distinguished FL from normal-mild status. From weighted data on 12,170 examinees we estimated associations between FL and sex-specific quintiles (Qs) of waist circumference (WC), waist-height ratio (WHtR), waist-hip ratio (WHR), waist-thigh ratio (WTR) and body mass index (BMI). From 5,289 examinees with morning observations we estimated FL's association with the lipid accumulation product (LAP; WC enlargement*fasting triglycerides). The population prevalence of FL was 18.5% (16% of women, 21% of men; 13% for ages 20-39, 24% for ages 40-74). FL prevalence was less (~7%) for low-adiposity adults [Q1 + Q2], regardless of the indicator. With adjustments for sex, age, ancestry, and high alcohol intake we compared the FL risk ratios for Q3, Q4, and Q5 (compared to [Q1 + Q2]) of each adiposity indicator. The highest Q5 risk ratio was for LAP (Q5RR 5.7 [95%CI 3.9–8.1]); the next was for WHtR (Q5RR 5.1 [4.2–6.0]). The lowest was for BMI (Q5RR 4.2 [3.5–5.1]). These rankings were similar for Q4 (Q4RR 2.8 for LAP, 2.6 for WHtR, and 2.4 for BMI). Continuous adiposity indicators ranked by area under the ROC curve (adjusted c-statistic) were LAP (0.765 [0.737–0.794]), WHtR (0.753 [0.735–0.772]), WC (0.753 [0.734–0.772]), BMI (0.746 [0.727–0.764]), WHR (0.727 [0.708–0.745]), and WTR (0.717 [0.699–0.736]). Quintile cutpoints for WHtR could guide low-cost programs to identify candidates for cardiometabolic evaluation or liver biopsy. Quintile cutpoints for LAP might improve the targeting of high-risk adults, but LAP requires an assay of fasting triglycerides.

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PRENATAL SOCIOECONOMIC INDEX IN RELATION TO ADULTHOOD FAT MASS AND FAT DISTRIBUTION. *Golareh Agha, Stephen Buka, Charles Eaton, E. Andrés Houseman, Karl Kelsey, Eric Loucks (Brown University, Providence RI 02912)

Numerous studies have reported associations between childhood socioeconomic position (SEP) and adulthood obesity, as measured by body mass index (BMI). However, very few studies have investigated SEP in early life, particularly during fetal development, in relation to directly assessed measures of fat composition in adulthood. Objectives were to examine whether prenatal socioeconomic index (SEI) is associated with central fat mass and fat distribution in adulthood. The study sample included 400 participants (mean age 48 y, 57% women) from the Longitudinal Effects on Aging Perinatal (LEAP) project, who are a subset of the New England Family Study. SEI was prospectively measured prenatally as a composite numerical score (range 0-100), using a weighted percentile of both parents' educational attainment, occupation, and income relative to the US population. Dual-energy x-ray absorptiometry (DXA) scans provided measures of central fat (android fat mass) and body fat distribution (android:gynoid fat mass ratio, trunk:limb fat mass ratio) at age 48 y. After adjustment for age, race, and maternal variables (pre-pregnancy BMI, age, marital status, smoking), prenatal SEI was inversely associated with all fat composition measures in women (for each 10 unit increase in SEI, β [95% confidence interval] = -1.62 [-2.67,-0.59], -0.02 [-0.04,-0.01], and -0.02 [-0.03,-0.01] for android fat mass, android:gynoid fat mass ratio, and trunk:limb fat mass ratio, respectively). No associations were observed in men. In conclusion, higher prenatal SEP was associated with having less centrally-located fat mass and less upper body-distributed fat in women but not men, consistent with other findings in the literature that show stronger associations between childhood SEP and obesity in women than men.

038-S

THE IMPACT OF BODY SIZE AND PHYSICAL ACTIVITY DURING ADOLESCENCE AND ADULT LIFE ON OVERALL AND CAUSE-EPECIFIC MORTALITY IN A LARGE COHORT FROM A MIDDLE-INCOME COUNTRY. *Arash Etemadi, Christian Abnet, Farin Kamangar, Farhad Islami, Hossein Poustchi, Sholom Wacholder, Paul Brennan, Paolo Boffetta, Reza Malekzadeh, Sanford Dawsey (National Cancer Institute, Bethesda MD 20852)

Most of the information about the association between obesity and mortality comes from Western populations. Reports from the low and middle-income countries show that leanness may be as important a determinant of mortality as obesity, but none have studied adolescence obesity, lifetime changes in body fatness, or physical activity. The Golestan Cohort Study is a population-based cohort in northeastern Iran in which 50,045 people above the age of 40 have been followed since 2004. People were shown a pictogram, validated in this population, to assess body size at ages 15, 30, and the time of recruitment, categorized from 1 (very slim) to 7 in men and 9 in women (very obese). Data on physical activity at these ages was also collected. Subjects were followed-up annually, and cause of death was determined. Cox regression models were adjusted for age at cohort start, smoking, socioeconomic status, ethnicity, place of residence, education, opium use and number of pregnancies. During 252,492 person-years of follow-up through December 2011, 2,529 of the participants died. The most common causes of death were cardiovascular disease (n = 1155, 45.7%), and cancer (n = 540, 21.4%). Larger body sizes at ages 15 or 30 in both sexes, and extreme leanness at age 15 in men, were associated with increased overall mortality. Physical activity level at these ages did not show any association with mortality. Moderate body size and more physical activity at cohort recruitment (age 40 and above) were associated with reduced mortality, after excluding deaths during the first year and adjusting for recent weight loss. Adolescents who lost weight, still had increased mortality from all medical causes and cancer. Weight gain after adolescence was associated with cardiovascular mortality. Mortality in this non-western population was independently associated with obesity, both during adolescence and early adult life, and cancer mortality was particularly affected by adolescent obesity.

039-S

GENDER DIFFERENCES IN ASSOCIATION BETWEEN SKIN-FOLD THICKNESS AND C-REACTIVE PROTEIN. *Abhishek Vishnu (Department of Epidemiology, University of Pittsburgh, Pittsburgh PA 15261)

Objective: C-reactive protein (CRP) is established as a marker of cardiovascular disease. However, determinants of high CRP in the general population are not known. Thus, association between triceps skin-fold thickness (SFT) and CRP was examined among adults (n = 2919) who participated in the National Health and Nutrition Examination Survey 2007-2008. Methods: Anthropometric and laboratory measurements were made using a standardized protocol. CRP values were converted to quartiles. Multivariable logistic regressions were used to estimate odds ratio (OR) for higher quartiles of CRP (reference = quartile 1) with increasing values of SFT, after adjusting for age, race, sex, BMI, and non-HDL cholesterol. Sex-stratified analysis was performed to test the association within each sex. Results: Women (n = 1464) as compared to men (n = 1455) had significantly higher SFT (23.6 mm vs. 14.9 mm, $p < 0.05$) and CRP (0.43 mg/dl vs. 0.30 mg/dl, $p < 0.05$). With each mm increase in SFT the odds for being in the highest vs. lowest quartile of CRP were 1.18 (95% CI 1.15, 1.22) in a sex-adjusted analysis, which attenuated but remained significant (OR =1.06; 95% CI 1.02, 1.10) after multivariable adjustment. In a multivariable and sex-stratified analysis, significant results were found among men (OR = 1.09; 95% CI 1.03, 1.16) but not among women (OR = 1.03; 95% CI = 0.98, 1.09). Further, when quartiles of CRP were regressed over quartiles of SFT, significant positive association was found among men (OR = 1.92, 1.57, 1.64 for quartiles 4, 3, 2 respectively vs. quartile 1 of SFT, p-trend <0.01) while the association was statistically insignificant among women (OR = 1.02, 1.18, 1.34 for quartiles 4, 3, 2 respectively vs. quartile 1 of SFT, p-trend = ns). Conclusion: While SFT is associated with CRP among men independent of traditional risk factors, this association is absent among women.

040

THE RELATIONSHIP BETWEEN HIGH RISK FOR OBSTRUCTIVE SLEEP APNEA SYNDROME AND GENERAL AND CENTRAL OBESITY: FINDINGS FROM A SAMPLE OF CHILEAN COLLEGE STUDENTS. *Adaeze Wosu, Juan Carlos Velez, Clarita Barbosa, Asterio Andrade, Megan Frye, Bizu Gelaye, Xiaoli Chen, Michelle Williams (Harvard School of Public Health, Boston MA 02115)

Objective: The purpose of this study was to assess the prevalence and extent to which high risk for obstructive sleep apnea syndrome (OSAS) is associated with general and central obesity among college students. Methods: We conducted a cross-sectional survey of 916 students attending four colleges in Punta Arenas, Chile. The students provided socio-demographic and lifestyle information, as well as information related to sleep apnea according to the Berlin Questionnaire. At study sites, investigators measured anthropometric and cardio-metabolic indices including weight, height, waist circumference, and blood pressure. General obesity was defined as BMI ~gt~ 30kg/m^2 (WHO criteria). Central obesity was defined as waist circumference ~gt~ 90 centimeters (cm) for men or waist circumference ~gt~ 80cm for women (International Diabetes Federation guidelines). Multivariate logistic regression models were fit to obtain adjusted odds ratios (OR) and 95% confidence intervals (CI). Results: The prevalence of high risk for OSAS, general obesity and central obesity were as follows: 7.8%, 12.8% and 42.7%. Students at high risk for OSAS had higher odds of general obesity (OR = 9.24, 95% CI: 4.51-18.94) and central obesity (OR = 2.78, 95% CI: 1.43-5.40) compared to those at low risk for OSAS. Conclusions: High risk for OSAS was strongly associated with general and central obesity.

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CONVENIENCE STORES AS A RISK FACTOR FOR OBESITY AMONG SMOKERS. *Masayoshi Oka, Jeff Gill, Dorothy K. Hatsukami, Naomi Breslau, Laura J. Bierut (Washington University School of Medicine, St. Louis MO 63110)

Previous studies have shown that neighborhood socioeconomic context, sub/urbanity, racial composition, and built environment are important neighborhood characteristics associated with health. However, there has not been a study that examined the multidimensional representations of neighborhood environments with obesity, particularly among smokers. Obese smokers have higher mortality risks, and thus are the high-risk population in the United States. In order to fill these important research gaps, we first conducted two separate robust principal component analyses to capture the variability of and neighborhood built environments and neighborhood sociodemographic characteristics. Neighborhood built environment variables were obtained from geographic information system (ArcGIS 10), and neighborhood sociodemographic variables were obtained from the 2005-2009 American Community Survey. We then conducted a series of Bayesian multilevel logistic analysis on obesity among 1,879 smokers aged 25-44 years who lived within the St. Louis Metropolitan area between 2003 and 2007. After accounting for the gradients in suburbanity and non-Hispanic black homogeneity, the associations of neighborhood built and social environments with obesity and the racial difference in obesity among smokers were attenuated. The increase in convenience store density remained associated with higher odds of obesity [odds ratio (OR): 1.20; 95% credible interval (CI): 1.04, 1.40], and the odds of obesity among non-Hispanic black declined from 2.36 (95% CI: 1.73, 3.20) to 2.03 (95% CI: 1.39, 2.96). Bringing neighborhood deprivation, suburbanity and non-Hispanic black homogeneity into the equation provides a comprehensive examination of neighborhood environments and obesity among smokers. Because obese smokers are the high-risk populations, future efforts need to modify the concentration and in-store contents of convenience stores.

042

PERCEIVED RACISM AND OBESITY INCIDENCE IN AFRICAN AMERICAN WOMEN. *Yvette Cozier, Jeffrey Yu, Patricia Coogan, Lynn Rosenberg, Julie Palmer (Slone Epidemiology Center at Boston University, Boston MA 02215)

Fifty one percent of African American women are obese compared with 33% of white women, and reasons for the disparity are not clear. Racial discrimination is a form of chronic stress that may influence weight gain. We prospectively assessed the association of perceived racism and obesity incidence in the Black Women's Health Study, which has followed approximately 59,000 U.S. black women since 1995 with mailed biennial questionnaires. In this analysis, 12,810 women under age 40 were followed from 1997 through 2009; during this time period, 4,315 women became obese (body mass index $\geq$ 30 kg/m2). Racism scores were created from questions asked in 1997 about the frequency of "everyday" racism (e.g., "people act as if you are dishonest") (5 questions) and of "lifetime" racism (i.e., unfair treatment on the job, in housing, by police). Experiences of racism were also assessed in 2009. Multivariable Cox proportional hazards models were used to estimate incidence rate ratios (IRRs) and 95% confidence intervals (CIs) for obesity in categories of the everyday and lifetime racism scores, adjusting for age, diet, exercise, and other lifestyle and neighborhood factors. The IRRs and 95% CIs in the highest compared to the lowest categories of the everyday and lifetime racism scores reported in 1997 were 1.31 (1.20-1.43) and 1.09 (0.98-1.22), respectively. Among women who reported the same levels of racism in 1997 and 2009, the IRRs and 95% CIs for the highest compared to the lowest categories of everyday and lifetime racism were 1.69 (1.45-1.96) and 1.38 (1.15-1.66), respectively. These findings suggest that experiences of racism contribute to the burden of obesity in U.S. black women.

043-S

RESIDENTIAL NEIGHBORHOOD, GEOGRAPHIC WORK ENVIRONMENT, AND WORK ECONOMIC SECTOR: ASSOCIATIONS WITH BODY FAT MEASURED BY BIO-ELECTRICAL IMPEDANCE IN THE RECORD STUDY. *Antoine Lewin, Basile Chaix (Institut National de la Santé et de la Recherche Médicale Unité 707 - Université Pierre et Marie Curie, Paris France)

Studies of associations between geographic life environment and obesity have mostly investigated body mass index and focused on residential neighborhoods. The present study examined associations between residential neighborhood, geographic work environment, and 11 work economic sectors and body composition [i.e. fat mass index (FMI) and percentage of fat mass (%FM)]. This study involved 4331 participants from the RECORD study, recruited in 2007-2008, and residing in the Paris metropolitan area, that where geolocated at their residence and at their workplace. Body composition was assessed by TANITA TBF 300 foot-to-foot bioelectrical impedance analyzers. Cluster analysis was applied to measure the socioeconomic status and urbanicity degree of the workplace and residential neighborhoods. Contextual variables for the residential and workplace neighborhoods and 11 work economic sectors were examined in relation to FMI and %FM using multilevel linear regression adjusted for individual factor. After adjusting for individual variables, FMI and %FM increased independently with decreasing density of population and educational level for men. Among women, only the residential educational level was related to FMI and %FM, with a stronger association than among men. Among women, FMI also independently decreased with the degree of urbanicity of the workplace neighborhood. Regarding working economic sectors, among men, a higher FMI and %FM was observed among participants working in the construction sector than among those working in the education sector. For women, FMI was lower among participants working in the construction sector than among participants working in the health and social sector. Public health programs attempting to reduce the obesity prevalence and social/territorial inequalities in obesity should consider, in addition to the residential neighborhood, the geographic environment around the workplace and the work economic sector.

044

THE EFFECT OF UNEMPLOYMENT ON BMI AND WAIST TO HIP CIRCUMFERENCE: EVIDENCE FROM THE SURVEY OF THE HEALTH OF WISCONSIN. *Lynne Morgan, Paul Peppard, Matt Walsh, Kristen Malecki (Survey of the Health of Wisconsin, Middleton WI 53562)

Unemployment can have negative impacts on general health including increased BMI leading to cardiovascular and other chronic diseases. This relationship has not been thoroughly studied among young adults. The aims of this study are to 1) Identify the association of unemployment on BMI and waist/hip circumference, and 2) Explore the possible protective effects of unemployment on young adults, including increased instance of eating in the home, and increased physical activity.Participants were identified using data collected by the Survey of the Health of Wisconsin, a cross-sectional, representations study of Wisconsin residents from 2008-2011. These individuals met the inclusion criteria of a) ages 21-35, and b) either employed full or part time, or unemployed but looking for work (n = 641). Unemployment in this population is 10.6%, with approximately half of those individuals falling under the federal poverty level based on household income. For young adults living below 100% of the FPL, unemployment decreases the likelihood of having a W2H ratio over 0.9 for men, 0.85 for women (Odds Ratio 0.51, 95% Confidence Intervals 0.17-1.54). Individuals above the FPL had an increased likelihood of having a high W2H ratio (OR 2.34, 95% CI 0.96-5.73) controlling for race, education, gender, comorbidities. Compared to employed participants, unemployed young adults under the FPL also ate fewer meals in the home (-1.53 95%CI -4.9-1.8) whereas participants above FPL ate more meals (+2.66, 95%CI 0.33-4.99). Whether or not a person's household income is below the Federal Poverty Level (FPL), has implications for how unemployment affects an individual's BMI and Waist-to-Hip (W2H) ratio. Though these results are not statistically significant, the demonstrated effect of a differential impact of unemployment on young adults whether or not they are below the poverty line indicates the need for future research on this population.

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DIET QUALITY AND RISK OF OBESITY AMONG YOUNG AFRICAN AMERICAN WOMEN. *Deborah Boggs, Lynn Rosenberg, Julie Palmer (Slone Epidemiology Center at Boston University, Boston MA 02215)

The prevalence of obesity (body mass index [BMI] ≥30 kg/m2) is highest among African American women, with most weight gain occurring before middle age. We prospectively assessed diet quality, as measured by the Alternate Healthy Eating Index-2010 (AHEI-2010), in relation to risk of obesity among younger women in the Black Women's Health Study, an ongoing follow-up study of 59,000 African American women aged 21-69 years in 1995. Dietary intake was assessed in 1995 and 2001 using food frequency questionnaires (FFQs); information on body weight and other lifestyle factors was ascertained every two years through mailed questionnaires. We restricted the analysis to 12,972 non-obese women aged <40 at baseline who completed both the 1995 and 2001 FFQs. AHEI-2010 scores were calculated by summing scores from 0 (worst intake) to 10 (best) for 11 dietary components: vegetables, fruit, whole grains, sugar-sweetened beverages, nuts/legumes, red/processed meat, *trans* fat, long-chain omega-3 fatty acids, polyunsaturated fat, sodium, and alcohol. Hazard ratios (HRs) and 95% confidence intervals (CIs) for incident obesity were estimated with Cox regression models, adjusted for age, baseline BMI, vigorous activity, and other lifestyle factors. During 16 years of follow-up, 5248 (40%) women became obese. The HR for incident obesity for the highest quintile of AHEI-2010 score relative to the lowest was 0.86 (95% CI 0.78-0.95). Of the dietary components, intake of red/processed meat was most strongly associated with obesity risk; the HR comparing the lowest intake quintile with the highest intake quintile was 0.80 (95% CI 0.73-0.88). Greater intakes of nuts/legumes and whole grains were also significantly associated with lower obesity risk but only among women with normal BMI at baseline. These results suggest that better adherence to the AHEI-2010 guidelines lowers obesity risk and that red meat accounts for much of the association among young African American women.

046

CAN BIRTH WEIGHT EXPLAIN DIFFERENCES IN THE ASSOCIATION OF INFANT GROWTH WITH SUBSEQUENT FAT FREE MASS BETWEEN POPULATIONS? *L L Hui, C Mary Schooling, Gabriel M Leung (School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Pokfulam Hong Kong SAR China)

Rapid infant growth is associated with subsequent adiposity. It has been suggested that infant growth promotes fat free mass (FFM) more than fat mass in developing countries giving extended windows during which catch-up growth may be beneficial in such settings where birth weight is typically low. We used multivariable linear regression to examine the association of birth weight and infant growth with FFM in 469 adolescents from the Hong Kong Chinese "Children of 1997' birth cohort who come from a population with a recent history of rapid economic development. Birth wieght was classfied as light (sex and gestational age specific z-score<0 or otherwise heavy). Infant growth was classified as rapid (change in weight z-score from birth to 12 months>0.67 or otherwise slow). FFM (kg) was assessed by dual energy X-ray absorptiometry (DEXA) at 15 years. Analysis was adjusted for sex, parental education and mother's place of birth. Compared with adolescents born light with slow infant growth, those with rapid infant growth had 4.9kg (95% confidence interval (CI) 3.1-6.6kg) more FFM if they were born heavy, and 2.3kg (95% CI 0.9-3.7kg) more FFM if they were born light. Adolescents born light who grew rapidly had similar FFM comparing to those born heavy who grew slowly. The differences in FFM by fetal and infant growth patterns were little changed by further adjusting for height. Both birth weight and infant growth made positive contributions to adolescent FFM, with no evidence that the association of infant growth with FFM varied with birth weight. Nevertheless, infant growth might make a greater contribution to FFM in developing countries where birth weight is lower than in developed countries where children born heavy may grow relatively slowly in infancy.

047

INFANT GROWTH AND ADOLESCENT ADIPOSITY – EVIDENCE FROM THE HONG KONG "CHILDREN OF 1997" BIRTH COHORT. *L L Hui, C Mary Schooling, Gabriel M Leung (School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Pokfulam Hong Kong SAR China)

Cardiovascular disease (CVD) is the leading cause of death. Influences throughout life affect long-term health and CVD risks. Infancy is potentially key window of developmental plasticity, and hence for intervention. We used multivariable linear regression to examined the association of infant growth with adiposity, proxied by body mass index (BMI), waist circumference, waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) at 13 years in a population representative Chinese birth cohort, "Children of 1997". We assessed the adjusted joint associations of size at birth (sex- and gestational age- specific birth weight z-score) and infant growth rate (change in weight z-score from birth to 12 months), using the lowest birth size and growth rate tertile as the reference, because infant growth is not independent of size at birth. In each birth weight category, a faster growth rate at 0-12 months was associated with a greater BMI and waist circumference in both boys and girls, adjusted for education, place of birth, BMI and height of parents. Compared with adolescents born small who grew slowly, those with high birth weight z-score (i.e. the 3rd tertile) and fast infant growth (i.e. the 3rd tertile) had on average the highest BMI (0.84 95% confidence intervals (CI) 0.58 to z1.10 for boys and 0.74 95% CI 0.49 to 0.99 for girls) and waist circumference (6.3cm 95% CI 4.2 to 8.4 for boys and 4.5cm 95% CI 2.5, 6.5 for girls) at 13 years, among boys they also had the highest WHtR (0.23 95% CI 0.01, 0.45). In contrast, birth weight z-score and infant growth were unrelated to WHR. Fast infant growth is associated with higher adolescent BMI but not higher adolescent WHR, suggesting that fast infant growth may result in general adiposity but not central adiposity at adolescence. How infant growth affects body composition, whether the associations vary by sex and whether associations observed during adolescence persist into adulthood remain to be determined.

048-S

A GENETIC IV ANALYSIS TO ASSESS THE EFFECT OF BODY MASS INDEX ON DEPRESSION IN THE HEALTH AND RETIREMENT STUDY. *Stefan Walter, Iván Mejía-Guevara, Eric J Tchetgen, Karestan Koenen, Ichiro Kawachi, Laura Kubzansky, M Maria Glymour (Harvard School of Public Health, Boston MA 02215)

Background: The relationship between adiposity and mental health remains controversial despite extensive prior observational research. We use a genetic risk score (GRS) as an instrumental variable (IV) to estimate effects of increases in body mass index (BMI) on depressive symptoms. Methods: Data are from 11842 (whites = 10322, blacks = 1520) individuals from the nationally representative Health and Retirement Study with data on a 10-item Center for Epidemiologic Studies Depression (CESD) scale and genetics collected in 2006 or 2008. Based on 32 Single Nucleotide Polymorphisms (SNPs) known to predict BMI, we calculated a GRS as the sum of the number of risk alleles multiplied by the per allele effect size on BMI (based on prior publications). We conducted over-identification tests with 4 IVs using subsets of the SNPs organized based on biological pathways (adiposity, appetite, and cardio-pulmonary factors) by which the genes might influence adiposity. Self-reported BMI prior to the assessment of CESD was used for validation of the external instrument. The CESD score was regressed on each genetic IV plus population stratification eigenvectors to derive the IV effect estimate. We compared these to conventional effect estimates derived from regressing CESD on self-reported BMI. Results: The GRS significantly predicted BMI in blacks ($r2 = 0.016$, $p < 0.001$) and whites ($r2 = 0.010$, $p < 0.001$). Self-reported BMI significantly predicted CESD, more strongly in whites (0.043, 95%-CI: 0.036, 0.05) than blacks (0.021, CI: 0.004, 0.038). IV effect estimates were large and statistically significant for whites (0.096, CI: 0.026, 0.167) but had very wide CIs for blacks (0.016, CI: -0.224, 0.256). Over-identification tests showed no evidence of possible pleiotropy in the genetic risk score. Conclusions: Our IV analysis reveals that genotypes associated with BMI are also associated with depressive symptoms in whites, supporting a causal effect of BMI on depression.

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RELATION OF ENDOGENOUS TESTOSTERONE LEVELS WITH CARDIOMETABOLIC RISK FACTORS IN THE REGISTRY OF HYPOGONADISM IN MEN (RHYME). *Julia Martha, Andre Araujo, Mario Maggi, Giulia Rastrelli, Thomas Hugh Jones, Teresa Curto, Raymond Rosen (New England Research Institutes, Inc., Watertown MA 02472)

Hypogonadism (HG) is a prevalent condition in men with broad health consequences. We examined the relation of endogenous testosterone (T) levels to cardiometabolic factors in RHYME, a registry of 999 men with clinically-diagnosed HG (naive to androgen treatment) from 25 sites in 6 European countries (DE/ES/IT/NL/SE/UK). T was measured centrally using mass spectrometry. Measurements for body mass index (BMI), waist and blood pressure (BP) (high BP = SBP ≥ 140 or DBP ≥ 90 mmHg) were recorded. Hypercholesterolemia, diabetes and medications were assessed by medical record. Other health-related factors were assessed by questionnaire. Unadjusted associations with T were assessed via Pearson's correlation coefficient (r) for continuous and t-tests for binary variables. Differences in geometric mean T (log-scale) in relation to cardiometabolic factors were assessed via multivariable linear regression models controlling for age, BMI, HG duration, smoking, physical activity, self-rated health, number of comorbidities, blood draw time and country. Mean age was 59 ± 10.5y and mean T was 9.5 ± 1.6 nmol/L, with significant variation by country (range: UK 9.9nmol/L; DE 11.8 nmol/L). Rates of obesity (44%), HBP (50%), hypercholesterolemia (31%) and diabetes (29%) were high. T was significantly correlated with BMI (r = -0.23) and waist (r = -0.20) but not BP. While more men with lower T were taking antihypertensive and lipid-lowering agents, the relation between T and high BP or hypercholesterolemia did not vary by medication use. Mean T levels were unrelated to other cardiometabolic factors or use of related medications in unadjusted or adjusted analyses. BMI did not modify the associations with T. Among men with diagnosed HG, endogenous T levels are strongly associated with body composition but not other cardiometabolic factors. Future analyses will examine the directionality of these associations and whether T therapy improves related outcomes in obese men with HG.

050-S

THE CAUSAL EFFECT OF OBESITY ON ANXIETY: GENETIC IV ANALYSES IN THE HRS STUDY. *Iván Mejía-Guevara, Stefan Walter, Eric J. Tchetgen, Ichiro Kawachi, Karestan Koenen, Laura Kubzansky, M. Maria Glymour (Harvard School of Public Health, Cambridge MA 02138)

Background: Prior observational research established that adiposity is associated with anxiety, but the size and direction of effects remain controversial. Recent genetic instrumental variable (IV) analyses investigated the relationship between body mass index (BMI) and common mental disorders and depression, but did not address anxiety specifically. Methods: Data are from 10907 (whites = 9627, blacks = 1276) participants in the Health and Retirement Study (HRS), a nationally representative cohort of US adults aged 50+ , with genetic data and 5 items from the Beck Anxiety Inventory. FTO and a genetic risk score (GRS), calculated as sum of 32 risk alleles multiplied by the per allele effect size on BMI (based on prior publications), were used as IVs. Self-reported BMI prior to the anxiety assessment was used to confirm that FTO and the GRS predicted BMI in HRS. We used separate-sample linear IV regression to investigate the causal effect of BMI on the anxiety score. Mechanism-specific GRS (e.g., adiposity, appetite, and cardio-pulmonary factors) were used for over-identification tests. Results: FTO and GRS explained between 0.3% and 1.5% of the variance in BMI in blacks and whites. In observational analyses, higher BMI predicted higher anxiety (whites, β per unit of BMI = 0.007, 95%-CI: 0.004, 0.009; blacks: β = 0.007, CI: 0.001, 0.013). The IV estimates based on FTO (white: 0.005, CI: -0.036, 0.047; blacks: 0.205, CI: -0.014, 0.423) and GRS (whites: -0.002, CI: -0.024, 0.019; blacks: 0.006, CI: -0.078, 0.090) were non-significant and close to the null. The over-identification test using mechanism specific GRS was rejected in blacks (p = 0.028) but not whites (p = 0.291) Conclusions: This IV analysis does not support a causal effect of BMI on anxiety. The rejected over-identification test in blacks may suggest that BMI is a heterogeneous phenotype with questionable causal interpretation or the existence of a common genetic determinant of BMI and anxiety.

051-S

ASSOCIATION BETWEEN PSYCHOLOGICAL DISTRESS AND UNINTENTIONAL NON-OCCUPATIONAL INJURIES AMONG U.S. ADULTS. Jana McAninch, *Christina Greene, Gordon Smith (University of Maryland, Baltimore MD 21201)

Background: Previous studies have demonstrated that individuals with mental illness have an elevated risk of intentional injuries, but the association between poor mental health and unintentional injuries is not well understood. Methods: We used the 2010 National Health Interview Survey to assess the association between psychological distress and the 3-month prevalence of unintentional non-occupational injury in adults. Psychological distress was measured by the Kessler Psychological Distress Scale, a validated scale that identifies community-dwelling persons with serious mental illness. Multivariable logistic regression was used to estimate adjusted odds ratios (AOR) and 95% confidence intervals. Results: Of the 27,157 participants, 2.5% (weighted %) reported a medically-attended unintentional injury in the past three months. Those with moderate and severe levels of psychological distress had 1.5 [1.2-1.9] and 2.1 [1.5-3.0] times higher odds of injury, respectively, as compared to those with low distress levels, after adjusting for age, sex, race, marital status, education level, alcohol use, physical functional limitation, presence of chronic disease, employment status, and health insurance status. Severe psychological distress was significantly associated with falls [AOR 2.3 (1.5-3.7)] and overuse/strain injuries [AOR 3.4 (1.4-8.1)] but not transportation-related injuries [AOR 1.7 (0.7-4.2)]. Conclusion: Among community-dwelling U.S. adults, psychological distress is significantly associated with unintentional non-occupational injury, and the magnitude of association increases with severity of distress. The association between psychological distress and injury may be particularly strong for fall and overuse/strain injuries. Screening for psychological distress to identify and intervene in high-risk groups should be considered as part of prevention strategies for both intentional and unintentional injuries.

052

EFFECTS OF MINIMUM LEGAL DRINKING AGE ON ALCOHOL AND MARIJUANA USE: EVIDENCE FROM TOXICOLOGICAL TESTING DATA FOR FATALLY INJURED DRIVERS AGED 16 TO 25 YEARS. *Guohua Li, Joanne Brady, Charles DiMaggio (Columbia University, New York NY 10032)

Alcohol and marijuana are among the most commonly used drugs by adolescents and young adults. The question of whether these two drugs are substitutes or complements has important implications for public policy and prevention strategies. Previous studies addressing this question are limited primarily to population-level data from self-reports and have produced conflicting results. Using data for drivers aged 16 to 25 years who were fatally injured within one hour of the crash in 13 states where toxicological testing was performed on a routine basis during 2005–2010 (n = 4,692), the authors assessed the effects of minimum legal drinking age (i.e., 21 years) on alcohol and marijuana use. Overall, 50.5% of the drivers studied tested positive for alcohol or marijuana (35.1% for alcohol only, 6.6% for marijuana only, and 8.8% for both drugs). Data on single drug use indicated that the prevalence of alcohol increased linearly from 13.7% at age 16 to 33.5% at age 20 years, and continued to rise at a slower pace after age 20, and that the prevalence of marijuana increased slightly from 6.2% at age 16 to 8.8% at age 20, and dropped markedly after age 20. The prevalence of combined use of alcohol and marijuana increased progressively from age 16 to 20 before leveling off. Multivariable relative risk modeling revealed that reaching the minimum legal drinking age was associated with a 17% increased risk of alcohol use (relative risk 1.17, 95% confidence interval 1.01–1.35) and a 16% decreased risk of marijuana use (relative risk 0.84, 95% confidence interval 0.56–1.27). These results suggest that alcohol and marijuana are substitutive drugs in adolescents and young adults.

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053-S

TIME TRENDS IN THE PREVALENCE OF ALCOHOL AND DRUGS IN FATALLY INJURED DRIVERS, 1999-2010. *Joanne Brady, Charles DiMaggio, Guohua Li (Columbia University, New York NY 10032)

Media attention and public concern regarding the role of drugs in motor vehicle crashes has grown in recent years. A previous study of drivers fatally injured in 2005-2009 found that almost 60% of the study sample tested positive for alcohol and other drugs (AOD) and nearly 20% tested positive for two or more drugs (including alcohol). Using data from the Fatality Analysis Reporting System, drivers who died within one hour of the crash in six states that performed toxicological testing on 80% or more of these drivers between 1999-2010 were examined. Over the 12-year study period, 53.0% of the 23,590 drivers studied tested positive for AOD (39.7% for alcohol, 24.8% for non-alcohol drugs, and 15.2% for two or more drugs (including alcohol)). While the prevalence of alcohol remained constant across the study period, the prevalence of non-alcohol drugs increased from 16.6% (95% confidence interval (CI) 14.8, 18.4) in 1999 to 28.3% (95% CI 26.0, 30.7) in 2010. From 1999-2010, stimulants were the most commonly detected drug class (10.4% (95% CI 10.0, 10.8)). Their use did not change meaningfully throughout the study period. Cannabis was the second most commonly detected non-alcohol drug and its prevalence more than doubled during the study period (from 5.3% (95% CI 4.8, 5.8) in 1999-2002 to 11.3% (95% CI 10.5, 12.0) in 2007-2010). Use of narcotics also increased considerably, particularly in female drivers and drivers aged 55-64 years. These results suggest that drugged driving, specifically driving under the influence of cannabis and narcotics, may be a contributing factor in an increasing number of fatal motor vehicle crashes.

054-S

PREVENTION OF SCUBA DIVING MISHAPS BY USING A PRE-DIVE CHECKLIST: A GROUPED RANDOMIZED TRAIL. *Shabbar Ranapurwala, Steven Wing, Petar Denoble (University of North Carolina, Chapel Hill, Durham NC 27707)

Scuba diving is a popular recreational activity that requires special skills and equipment for extended underwater stay. Mishaps in this environment may lead to injuries, permanent disabilities and fatalities. Diving mishaps are unwanted and unplanned events that increase the risk of an injury. Divers Alert Network conducted a grouped randomized trial in summer 2012 to study the effect of using a pre-dive checklist of safety procedures on the incidence of diving mishaps in recreational scuba divers. We collected data from four popular dive sites. Location-days were randomized; all the enrolled divers on a day were either in the intervention or control group. Each diver could participate only once. The study included 70 location-days and recruited 1080 divers who contributed 2043 dives. A post dive questionnaire evaluated the incidence of diving mishaps. Poisson regression models were used to compare rates of mishaps in different groups. Further analysis to control for the correlation between divers who were randomized to a research arm on the same location-day shall be conducted using generalized estimating equations (GEE). The crude mishap rate for the intervention group was 17.5 (95% CI: 15.3, 20.0) per 100 dives and for the control group was 22.2 (95% CI: 19.2, 25.6) per 100 dives. The crude rate ratio of mishaps for divers in the intervention group was 0.79 (95% CI: 0.65, 0.96) as compared to the control group. Reduction of diving mishaps indicates that a pre-dive check may lead to better and safer recreational diving experiences.

055

POTENTIAL BIAS IN ASSIGNING CRASH RESPONSIBILITY USING MOVING VIOLATIONS. *Allison Curry, Melissa Pfeiffer, Rachel Myers, Michael Elliott (Center for Injury Research and Prevention, The Children's Hospital of Philadelphia, Philadelphia PA 19002)

Two common methods used to assign driver responsibility for a motor vehicle crash are based either on the issuance of a citation for a moving violation or the presence of a driver-related crash-contributing factor. Our objective was to understand the practical implications of using these alternative methods, in particular in the context of young novice driver crashes. The study sample included all drivers involved in a police-reported crash with a New Jersey provisionally licensed driver under 21 years of age from 1/1/08 to 5/31/11 (n = 155,473). We excluded hit-and-run crashes and crashes involving a pedestrian, pedalcyclist, or non-passenger vehicle. Police crash reports included information on moving violations issued to each driver and 14 specific driver actions that may have contributed to the crash (e.g., unsafe speed, failure to obey traffic control device). Crash investigators were instructed to select for each driver the most prominent factors (up to two) contributing to the crash. We utilized proportions and chi-square tests to determine the concordance between issuance of a moving violation and presence of a driver action. 50.0% of all crash-involved drivers were assigned at least one crash-contributing driver action, while 17.0% were issued a moving violation. Of those assigned at least one crash-contributing driver action, 69.4% were not issued a moving violation. On the other hand, only 8.6% of drivers issued a moving violation had no driver action reported. Further, given the presence of a crash-contributing driver action, young provisional drivers were cited for a moving violation more often than non-provisional drivers (32.1% vs. 26.0%, $p < 0.001$). Studies that rely on moving violations from police crash reports to assign crash responsibility, for example those utilizing induced exposure techniques, should thoughtfully consider potential resulting biases as this method may severely underestimate the number of responsible drivers.

056-S

RISK FACTORS OF FALL-RELATED INJURIES AND THE INTERACTION OF BONE MINERAL DENSITY (BMD) AND HEALTH BEHAVIORS. *Dohee Lim, Won Kyung Lee, ChoungAh Lee, Namsoo Park, Hyesook Park (Ehwa Womans University College of Medicine, Seoul South Korea)

Objective: The aim of this study is to examine the difference in the risk of fall-related injury according to bone mineral density (BMD).And features in health behaviors affecting to the risk of fall-related injury by interaction with BMD is investigated. Methods: Secondary and tertiary data (2008-2009) with BMD checkups among fourth Korean National Health and Nutrition Examination Survey data is used to examine the relation of fall-related injury and BMD with demographic sociological features. The risk of fall-related injury according to BMD is analyzed by logistic regression model and the relation between BMD and health behavior is analyzed by chi-square test and multinomial logistic regression analysis. The interaction between BMD and health behavior is detected by comparing expected joint odds ratio and observed joint odds ratio, based on Additive model and Multiplicative model. Results: In the whole population, the risk of fall-related injury according to BMD is not significantly different. However, the risks of fall-related injury with low BMD in the aged over 65 years old group (OR = 3.30(1.03, 10.59)) and postmenopausal women(OR = 3.09(1.26, 7.60) are three times higher or more than normal BMD. In addition, drinking, obesity and smoking show interaction with BMD in the risk of fall-related injury, that increase the risk compared to individual effects. Conclusion: The groups of aged over 65 years old and postmenopausal women with low BMD need to be classified into a high-risk group for fall-related injury and managed for prevention. Drinking, smoking, physical activity and weight are health behaviors related to BMD, of which should be controlled to prevent fall-related injury.

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PHYSICAL HEALTH CONSEQUENCES OF BEING INJURED DURING THE WORLD TRADE CENTER TERRORIST ATTACKS ON SEPTEMBER 11, 2001. *Robert Brackbill, Mark Farfel, James Cone, Steven Stellman (Department of Health and Mental Hygiene, Long Island City NY 11101)

Few studies have focused on injuries from World Trade Center (WTC) disaster on September 11, 2001 (9/11), although there were probably more severely injured persons than initially recognized. Severe unintentional injury has physical, functional, and mental health consequences including elevated mortality 10 years post injury and risk for mental health problems such as posttraumatic stress disorder (PTSD). The WTC Health Registry identified 10,779 persons with no pre-existing chronic health conditions pre-9/11 who were present during and soon after the WTC attacks, 2,578 of whom reported sustaining 1 or more types of injury (including sprain/strain, broken bone, burn, laceration, and head injury). Survey data obtained during 2003-04 and 2006-07 were used to assess the odds of reporting diagnosed chronic conditions up 2 to 6 years after 9/11. Number of injury types and probable PTSD (2003-04) were significantly associated with any post 9/11 diagnosed chronic condition. Persons with 3 injury types and PTSD had a 5-fold higher risk of heart disease (adjusted odds ratio = 4.9, 95% confidence interval: 2.3-10.4) while PTSD only had an AOR = 2.6 (1.8, 3.7) compared with those with no injury and no PTSD. Among those without post 9/11 PTSD, 1 injury type was significantly associated with heart disease (AOR = 1.9, 1.4-2.7) and with respiratory disease (AOR = 1.5, 1.3.-1.8), but not with other conditions. No PTSD and 3 injury types had an AOR = 2.8 (1.7-4.8) association with respiratory disease. Although the underlying mechanisms of these associations are unclear, this study demonstrates elevated risk of chronic disease up to 6 years after being injured on 9-11-01 among injured persons with or without comorbid PTSD; clinicians should be aware of heightened health risk among injured disaster victims.

058-S

THE ROLE OF SEX AND SYMPTOM SEVERITY IN SPORTS-RELATED CONCUSSION: A SURVIVAL ANALYSIS. *Jennifer Reneker, Lynette Phillips (Department of Epidemiology and Biostatistics, College of Public Health, Kent State University, Kent OH 44242)

Investigative efforts have increased over the past decade in order to reveal the mystery of a once regarded benign injury: sports-related concussion. This has now been identified as a substantial public health concern. The purpose of this study is to: 1) determine if there are differences between males and females in each of the following time-to-event variables: days to assessment, days of medical treatment, and days from the concussion to discharge and, 2) determine if athletes with greater symptom severity, as measured by the Post-Concussion Symptom Scale (PCSS), at initial assessment have differences in each of these time-to-event variables. This study was conducted on a clinical dataset of 106 (69 male and 37 female) student athletes with diagnosis of concussion, mean age of 15.3 years. The data was obtained by retrospective chart review from a pediatric sports-medicine clinic. Kaplan-Meier survival analyses and Cox-Proportional Hazard (CPH) analyses were completed to estimate the effect of sex and PCSS score on each time-to-event variable. Within the sample of males, those with higher PCSS scores had fewer numbers of days-to-assessment ($p = .04$), however those with lower PCSS scores had more days between the concussion and discharge from medical care ($p = .05$). For females, there were no differences by PCSS score for any of the variables of interest. The results of the multivariable CPH regression analysis revealed no significant findings by sex for days to assessment with all potential confounders controlled. There were however, significant findings indicating females had less days of medical treatment (hazard ratio .53, 95% CI: .34, .81) and less days total (HR .56, 95% CI: .37, .85) controlling for all potential confounders. This study on clinical data provides new insight into sports-related concussion and demonstrates differences in the influence of symptom severity on time-to-event variables in males and females.

059-S

HOME ENVIRONMENT-RELATED FACTORS ASSOCIATED WITH THE FAMILY-DOG BITING A CHILD LIVING IN THE SAME HOME. *Locksley L McV Messam, Phillip H Kass, Bruno B Chomel, Lynette A. Hart (University of California Davis, Davis CA 95616)

Few studies have examined risk factors for bites by the family dog to persons living in the same home. This veterinary clinic-based retrospective cohort study was aimed at identifying canine environmental risk factors for bites by the family dog to children aged five to fifteen years and living in the same home as the dog. Data were collected by interviewer-administered questionnaire from veterinary clients in the waiting room of clinics in Kingston, Jamaica (236) and San Francisco, USA (61). Exposures of interest were factors relevant to the dog's living environment. Dog bites, in the two-year study period, included those occurring both while the children were (20) and were not playing (9) with the dog and exposure information pertained to the period preceding the dog bite incident. Data were analyzed using binomial regression in SPSS version 20, with confounders selected using directed acyclic graphs and the change-in-estimate procedure. No heterogeneity by city of origin was found and thus data from both cities were pooled for final analyses. Dogs living in homes having no outside yard space (4%) were at higher risk (RR = 3.0; 95% CI: 0.9-9.8) for biting than dogs living in homes that had. Additionally, dogs that were allowed inside (64%) the home (RR = 3.0; 95% CI: 1.0-8.6) and dogs routinely allowed to sleep in the bedroom (23%) of a family member (RR = 3.9; 95% CI: 2.0-7.9) were also at higher risk for biting than those that were not. Finally, dogs that could leave the premises unaccompanied (16%) were at higher risk (RR = 2.8; 95% CI: 1.4-5.7) for biting than those that could not. While a study with a larger sample size is necessary to detect possible heterogeneity by city, these elevated RRs generally suggest that family dogs living in closer physical proximity to members of the family may be at elevated risk for biting children living in the same home.

060

CONDITIONAL AND UNCONDITIONAL INFECTIOUSNESS EFFECTS IN VACCINE TRIALS: THE RELATION AND ESTIMATION. *Yasutaka Chiba, Masataka Taguri (Kinki University School of Medicine, Osaka Japan)

Even if a person is infected irrespective of the vaccine, the vaccine may impair the ability of the infectious agent to initiate new infections; i.e., make the agent less infectious. This mechanism is sometimes referred to as an infectiousness effect. Recently, two definitions of the infectiousness effect were proposed using causal inference theory: conditional and unconditional effects? (Epidemiology 2012; 23: 751-761). Here, we demonstrate a relationship between these two infectiousness effects, and propose a simple estimation method for the effects. We consider a setting in which each household consists of two persons, where the first person is randomized to receive a vaccine or a control, and the second person receives nothing. In this setting, we require the following two assumptions: (i) the second person cannot be infected unless the first person is infected, and (ii) there is no household in which the first person would be infected if vaccinated, but uninfected if unvaccinated. We show that, under these two assumptions, the unconditional effect is equal to the conditional effect on the risk ratio scale. Thus, a common method can be applied to estimate these two effects. To derive the estimation method, we require an additional assumption that there is no unobserved baseline covariate that affects the infection statuses of the two individuals. With this additional assumption, we show that the estimation can be achieved by estimating the average causal effect of the vaccine status of the first person on the infection status of the second person with the vaccine group as the target population, where only data in which the first person was infected is used.

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APPLYING SYSTEM DYNAMICS MODELING TO EPIDEMIOLOGICAL RESEARCH: AN EXAMPLE OF PSA SCREENING. *Anton Palma, David Lounsbury, Nicolas Schlecht, Ilir Agalliu (Albert Einstein College of Medicine, Bronx NY 10461)

System Dynamics (SD) is a novel mathematical modeling approach that can be used to simulate intervention trials and explore alternative scenarios that would not otherwise be possible (counterfactual conditions). Recently the U.S. Preventive Services Task Force recommended against prostate-specific antigen (PSA) screening for prostate cancer. However, evidence for PSA screening from two recent prostate cancer screening trials: the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, and the European Randomized Study of Screening for Prostate Cancer (ERSPC), is inconsistent, with the ERSPC trial reporting a significant benefit where the PLCO trial did not. Differences in compliance, contamination rates and PSA screening thresholds have been proposed to explain the discrepancies. We applied SD modeling to conduct a combined evaluation of outcomes from these two trials to further explore the utility of PSA screening at population level and examine the impact of hypothetical scenarios that correct for the above inconsistencies.We first reproduced the PLCO trial results for 13 year follow-up. Then, we applied the contamination rate (i.e., use of PSA testing) in the ERSPC control arm to the PLCO trial control arm. Initial SD model results indicate that correcting for contamination rate in the PLCO trial yields a relative risk (RR) of 0.86 (95% CI 0.68-1.08) for prostate cancer-specific mortality after 13-year follow-up, a risk reduction of 14% compared to published PLCO trial results. Further work will examine the impact of adjusting for differences in PSA screening frequency (quadrennial vs. annual) and thresholds (3 vs. 4 ng/ml) between trials, as well as extrapolation of results to 20 years of follow-up. The utility of SD in simulating epidemiological data and exploring alternative hypothetical scenarios make it a powerful tool for sensitivity analysis, data synthesis and study design with potential implications for policy change.

062

CAUSAL INFERENCE IN EPIDEMIOLOGY USING BAYESIAN METHODS: THE EXAMPLE OF META-ANALYSIS OF STATINS AND FRACTURE RISK. *Lawrence McCandless (Simon Fraser University, Burnaby BC Canada)

Numerous epidemiologic studies indicate that statin use reduces the risk of fractures in the elderly. However, a causal relationship is not supported by data from randomized trials. Healthy user bias is implicated as a likely culprit for the controversy. It is a type of unmeasured confounding that results from failure to measure and adjust for patient-level tendencies to engage in healthy behaviours (e.g. use of alcohol and tobacco). In this presentation, I will summarize the evidence supporting an association between statins and fractures, and then explore sensitivity to bias from confounding using Bayesian techniques. I will draw parallels with bias modelling in observational studies, discuss prior distributions, and discuss other issues including selection bias, publication bias, and the "decline" effect.

063

NEIGHBORHOOD CONTRIBUTIONS TO RACIAL/ETHNIC OBESITY DISPARITIES AMONG NEW YORK CITY ADULTS. *Sungwoo Lim, Tiffany Harris (New York City Department of Health and Mental Hygiene, Queens NY 11101)

Neighborhood plays an important role in racial/ethnic obesity disparities. Multilevel modeling is often used to estimate neighborhood effects, but requires stringent conditions to properly address neighborhood confounding and complex sampling. Using innovative methods, the authors sought to determine 1) the total influence of neighborhood confounding on racial/ethnic obesity disparities in New York City (NYC) after accounting for complex sampling and 2) how much each neighborhood factor (walkability, percent of blacks, poverty) contributed to this effect. Three-year Community Health Survey data (2002-4) were combined with Census 2000 zip code-level data. Odds ratios (ORs) for obesity were determined using two sets of regression analyses. First, the method incorporating the conditional pseudolikelihood into complex sample adjustment was used. Second, ORs for race/ethnicity from a conventional multilevel model with each neighborhood factor were compared with those from a hybrid multilevel model. In the first analysis, the weighted OR for blacks versus whites (OR = 1.82, 95% confidence interval (CI) = 1.64-2.02) was attenuated when full neighborhood confounding was controlled for (OR = 1.42, 95% CI = 1.22-1.64). In the second analysis, percent of blacks represented almost the entire neighborhood effect whereas the walkability contribution was minimal. Living in certain NYC neighborhoods explained a large portion of obesity disparity between blacks and whites. Unlike most multilevel studies, this finding is generalizable to the NYC population. Neighborhood segregation played a major role in explaining the NYC racial/ethnic obesity disparities. The study highlights an importance of estimating a valid neighborhood effect for public health surveillance and intervention.

064

MULTIPLE IMPUTATION ANALYSIS OF NESTED CASE-CONTROL AND CASE-COHORT STUDIES. *Hisashi Noma, Shiro Tanaka, Sachiko Tanaka, Shizue Izumi (The Institute of Statistical Mathematics, Tokyo Japan)

The nested case-control and case-cohort designs are common means of reducing the cost of covariate measurements in large failure-time studies. Under these designs, complete covariate data are collected only on the cases (i.e., subjects whose failure times are uncensored) and some matched controls selected using risk-set sampling or a subcohort randomly selected from the whole cohort. In many applications, certain covariates are readily measured on all cohort members, and surrogate measurements of the expensive covariates may also become available. Using the covariate data collected outside the selected samples, the relative risk estimators can be improved substantially. In this study, we discuss a unified framework for the analysis of these designs using the multiple imputation method, which is a well-established method for incomplete data analyses. The multiple imputation method is currently available in many standard software, and is familiar to practitioners in epidemiologic studies. In addition, this multiple imputation method uses all the data available and approximates the fully efficient maximum likelihood estimator. We also discuss parametric and nonparametric approaches for modeling the distributions of missing covariates: the Markov Chain Monte Carlo method for the Cox regression model by Chen et al. (Biometrika 2006; 93: 791-807) and the approximate Bayesian bootstrap. Simulation studies demonstrated that in realistic settings, the multiple imputation estimators had greater precisions than existing estimators. Illustrations with data taken from Wilms' tumor studies are provided.

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IMPROVEMENT OF 1:M MATCHING USING AN ADAPTIVE ALGORITHM: PROOF OF CONCEPT. *Til Sturmer, Richard Wyss, Virginia Pate, Kenneth J. Rothman (University of North Carolina at Chapel Hill, Chapel Hill NC 27599)

The goal of individual cohort matching is to create matched sets comprising exposed and unexposed subjects in which the matching covariate has nearly the same value for all subjects in the matched set. The precision of the ensuing exposure effect estimate can be increased by increasing the number of unexposed individuals matched to each exposed one (1:M matching). In theory, residual confounding bias could be reduced with 1:M matching by choosing consecutive unexposed matches that take the covariate value of the previous unexposed matches into account to maximize similarity between the covariate value for the exposed person and an overall measure of central tendency, such as the mean, for the corresponding matched unexposed persons. We simulated cohort studies with 2 dichotomous and 2 continuous covariates affecting a dichotomous exposure via a logit link, and all these affecting a Poisson distributed recurrent outcome. Two additional covariates only affected either exposure or outcome. Random 1:M matching by propensity score (PS) was implemented using two different calipers (± 5 on the second decimal place of PS and ½ of the standard deviation of logit (PS)) and exposure prevalences (0.2 and 0.04). The caliper midpoint for the Mth unexposed match was either kept at the value of the exposed (conventional non-adaptive) or adjusted so that the mean of all M unexposed matches would be the same as the value in the exposed if the Mth unexposed match had exactly the midpoint value. Adaptive 1:M matching outperformed non-adaptive (conventional) 1:M matching in all scenarios assessed. Bias and MSE reduction ranged from 44%-93% and 8%-45%, respectively. Adaptive matching led to an almost monotonic decrease in residual confounding bias with increasing M. We conclude that adaptive 1:M matching can reduce residual bias. However, parameters affecting bias reduction achieved by adaptive matching need to be identified before widespread use can be recommended.

066

A NEW INDICATOR OF INFLUENZA INCIDENCE BASED ON VIRAL AND INFLUENZA-LIKE ILLNESS SURVEILLANCE DATA. *Ivo Foppa, Sue Reynolds (Centers for Disease Control and Prevention; Atlanta GA 30329)

Quantification of the excess mortality due to seasonal influenza viruses relies on the an indicator of influenza incidence throughout the year. Currently, the proportion of samples submitted to the National Respiratory and Enteric Virus Surveillance System (NREVSS) that test positive for specific influenza types/subtypes, is most commonly used for that purpose. This measure, however, is a measure of relative frequency (among all causes of acute respiratory infection) rather than of absolute frequency and may therefore bias the resulting estimates. We propose a new indicator of influenza incidence that is composed of the conventional proportion positive and of the number of visits due to influenza-like illness (ILI) per provider as reported in the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet). We theoretically justify the indicator and show under what assumptions it is an unbiased measure of influenza incidence.

067

USING RESTRICTION TO CONTROL UNMEASURED CONFOUNDING IN PHARMACOEPIDEMIOLOGY. *Mike Jackson (Group Health Research Institute, Seattle WA 98101)

Observational drug safety/effectiveness studies often use large, linked administrative healthcare data systems. Much research has focused on methods for adjusting for confounding when using these data systems. However, important confounders related to healthcare utilization are often not captured by these data systems, which can cause spurious results in drug studies, even when using state-of-the-art adjustment methods. In contrast to adjustment, restricting the study population on selected variables may reduce confounding by unmeasured variables that are correlated with the restriction variables. We explored the use of restriction to control unmeasured confounding in the association between influenza vaccination and risk of pneumonia. This is a useful test case, because (a) time periods when influenza does not circulate provide a control period when the true association is known to be null, and (b) confounding in the influenza/pneumonia association has proven intractable to any adjustment based on administrative data. In a cohort of seniors followed for three years, we found strong confounding: prior to the circulation of influenza, vaccinated seniors were 32% less likely to develop pneumonia than unvaccinated seniors (hazard ratio [HR], 0.68) after adjusting for age and sex. Even after adjusting for measurable data using a high-dimensional propensity score did not reduce this confounding (adjusted HR, 0.68). In contrast, restricting the population on two variables (use of home oxygen and use of antipsychotic medications) removed half of the confounding (age- and sex-adjusted HR in restricted population, 0.82). This restriction only excluded 3.3% of the total cohort. These results show that restriction has the potential to be a powerful tool for observational pharmacoepidemiology, if generalizable techniques can be developed for identifying useful restriction variables.

068-S

IDENTIFYING IMPLAUSIBLE TRAJECTORIES IN LONGITUDINAL DATA. *Melinda C. Power, Susan Korrick, Francine Grodstein, Howard Hu, Bernard Rosner, Marc G. Weisskopf (Harvard School of Public Health, Boston MA 02115)

Longitudinal data analysis is increasingly common in epidemiologic studies and presents several unique challenges. One such challenge is the potential for implausible outcome trajectories to bias study results in much the same way implausible data points may bias results. Using real data, we describe a method to identify impossible or implausible data trajectories when an outcome has a generally expected direction of change over time. Specifically, we use an adaptation of the generalized extreme studentized deviate procedure and compare results obtained with and without inclusion of data that creates an implausible trajectory. In our motivating example of a study of the association between lead exposure and change in cognitive function in a subset of participants from the Nurses' Health Study (n = 584), we identified one participant with implausible improvement on several cognitive tests. After exclusion of implausible data, the magnitude of negative associations between tibia bone lead concentrations and change in cognitive test scores—considering each test individually—increased considerably for those tests where we had identified a pattern of implausible improvement. Similar results were found for summary scores of total cognition (beta before exclusion: -0.014, beta after exclusion: -0.024) and verbal memory (beta before exclusion: -0.006, beta after exclusion: -0.017). While overall study conclusions remained similar despite substantial changes in point estimates, we expect changes of similar magnitude are likely to change study conclusions in other settings. We conclude with a discussion of alternate strategies for identification of implausible trajectories in repeated measures data and when use of such strategies to exclude implausible data as part of the data cleaning process may be desirable.

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069-S

USING BOOTSTRAP METHODS FOR CONFIDENCE INTERVAL ESTIMATION IN EPIDEMIOLOGIC RESEARCH. *Ashley Naimi, Jay Kaufman, Erica Moodie (McGill University, Montreal QC Canada)

The bootstrap is a well-known alternative for confidence interval (CI) estimation. We assess the performance of two-sided 95% maximum likelihood (ML)-based and a bias corrected (BC) bootstrap CI estimator in simulated and empirical data. We simulated data from a Cox regression model with a single binary exposure and confounder with event rates of 0.02, 0.05, 0.1, 0.2, 0.5, 0.8, 0.9, 0.95, & 0.98, and samples sizes of 100, 500, 1000, & 1500. We assessed CI performance using coverage and median confidence limit ratio (mCLR). We used 250, 500, 1000, & 2000 bootstrap resamples. The coverage range for ML-based and BC CIs was 0.40 to 0.95 and 0.80 to 0.95, respectively. The mCLR range for ML-based and BC CIs was 1.2 to 6.8 and 1.2 to 9.0, respectively. In moderate to large samples and event rates, ML-based and BC CIs did not differ. In small samples and event rates BC CIs had better coverage properties with slightly larger CLRs. Importantly, BC CIs did not differ by number of resamples used. Next, we used 3 empirical studies to explore CLRs of ML and bootstrap CIs: i) a comparison of cleansing solutions on time from admission to infection or discharge for burn patients (n = 154; infection rate: 1.4 per 100 person-weeks); ii) a National Longitudinal Survey of Youth (NLSY) study to evaluate the relation between poverty status and time to weaning of first-born children (n = 927; weaning rate: 5.9 per 100 person-months); and iii) a NLSY study to evaluate the relation between breast-feeding (ever versus never) and hospitalization for pneumonia in the first year of life (n = 3470; hospitalization rate: 0.2 per 100 person-months). CLRs for ML-based and BC CIs for the burn data were 3.5 & 5.3, respectively; for the weaning data both CLRs were 1.5; for the pneumonia data, the CLRs were: 3.4 & 3.7, respectively. Negligible changes were observed for different number of resamples. Similar results were observed for Wald, percentile, and accelerated bootstrap CIs.

070

PROPORTIONAL AND NON-PROPORTIONAL SUBDISTRIBUTION HAZARDS REGRESSION USING SAS. Maria Kohl, Karen Leffondré, *Georg Heinze (Medical University of Vienna, Vienna Austria)

We consider a study on determinants of progression of chronic kidney disease, where the outcome is time to dialysis, with death as competing event. Some of the risk factors show time-dependent effects on the subdistribution hazard causing misspecification of a proportional subdistribution hazards (PSH) regression model. We present a new SAS macro %PSHREG that can be used to fit a PSH model but also accommodates the possibility of non-PSH. Our macro first modifies the input data set appropriately and then applies SAS's standard Cox regression procedure, PROC PHREG, using weights and counting-process format. With the modified data set, standard methods can then be used to estimate cumulative incidence functions for an event of interest. In general, proportional cause-specific hazards do not ensure PSH. In case of non-PSH, random censoring usually distorts the estimate of the time-averaged subdistribution hazard ratio of a misspecified PSH model, as later event times are underrepresented due to earlier censoring. To address this issue, we can optionally weight the summands of the estimating equations, i.e., the risk sets at each event time, by inverse-probability-of-censoring or by number-at-risk expected had censoring not occurred. While the former weights make time-averaged effect estimates independent from the observed follow-up distribution, the latter allow an appealing interpretation of the average subdistribution hazard ratio as 'odds of concordance' of time-to-dialysis with the risk factor. We illustrate application of these extended methods for competing risks regression using our macro, which is freely available at http://cemsiis.meduniwien.ac.at/en/kb/science-research/software/statistical-software/pshreg/, by means of analysis of our motivating example.

071-S

MENDELIAN RANDOMIZATION IN HEALTH RESEARCH: USING APPROPRIATE GENETIC VARIANTS AND AVOIDING BIASED ESTIMATES. *Amy Taylor, Neil Davies, Jennifer Ware, Tyler VanderWeele, George Davey Smith, Marcus Munafo (University of Bristol, Bristol UK)

The use of Mendelian randomization for assessing causal relationships in epidemiological studies is becoming widespread. In order for the results of Mendelian randomization studies to be valid, there must be robust evidence, external to the study in question, that the genetic variants are associated with the exposure of interest. Using a specific example centered on tobacco research, we use simulated data to demonstrate how results can be biased if researchers select genetic variants on the basis of their association with the exposure in their own dataset, as often happens in candidate gene analyses. This can lead to estimates that indicate apparent causal relationships, despite there being no true effect of the exposure on the outcome, or over-estimation of the magnitude of true causal effects. In addition, we illustrate that if researchers use a poor proxy for a true underlying exposure, such as cigarettes per day for lifetime tobacco exposure, they can obtain incorrect estimates of the effects of the underlying exposure on the outcome in instrumental variable analysis. Mendelian randomization is a potentially valuable tool to help understand the etiology of disease. Researchers will only realize this potential if they base their studies on well-characterized variants and are cautious about making inferences about magnitudes of the relationships between phenotypes and outcomes.

072

FORMALIZING THE ROLE OF COMPLEX SYSTEMS APPROACHES IN CAUSAL INFERENCE AND EPIDEMIOLOGY. *Brandon Marshall, Sandro Galea (Brown University, Providence RI 02912)

There have been several calls for the adoption of complex systems approaches in epidemiology and public health. This work has largely centered around the potential for such methods to examine disease etiologies with a high degree of complexity, characterized by non-linear feedback behavior, threshold dynamics, and multiple interacting effects. In this paper we make an explicit effort to reconcile complex systems methods with modern thinking in causal inference, and show that these approaches should rely on counterfactual outcome frameworks to define complex causal "webs". Further, systems science methods can be formalized in a manner analogous to those developed for current analytic techniques to achieve causal inference. Using as an example an agent-based model constructed to represent HIV transmission in a dynamically evolving risk network, we demonstrate that complex systems models can be used to simulate counterfactual outcomes, providing an alternative technique to stratification-based and G-methods approaches for determining disease causes. Thus, complex systems methods (and simulation approaches broadly) represent a methodological bridge between studies that produce estimates of average causal effects and unobserved counterfactual outcomes. We show that these models are of particular utility, and perhaps the only viable solution, when the hypothesized causal mechanisms are of sufficient complexity such that the assumptions of modern empirical-based methods (e.g., marginal structural models) cannot be met. Finally, we will describe the set of assumptions that must be satisfied to ensure that the results of complex systems models represent average causal effects. Although not without challenges, complex systems methods represent a promising set of novel approaches to identify and evaluate causal effects, and are thus well suited to complement other modern epidemiologic methods of etiologic inquiry.

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073-S

REPORTING OF INSTRUMENTAL VARIABLE ANALYSES IN COMPARATIVE EFFECTIVENESS RESEARCH. *Sonja Swanson, Miguel Hernan (Harvard School of Public Health, Boston MA 02115)

Instrumental variable (IV) methods are becoming mainstream in comparative effectiveness research, yet such methods rely on radically different assumptions than traditional epidemiologic methods. Specifically, IV methods require a variable that meets three conditions: (1) it is associated with treatment (2) it does not affect the outcome except through treatment, and (3) it does not share any causes with the outcome. To obtain a point estimate, an untestable fourth condition must also be met. In order to assess whether these conditions were conveyed appropriately in the literature, we performed a systematic review of observational studies using IV methods to estimate effects of relatively well-defined medical interventions. After obtaining 2,269 unique publications from PubMed, Embase, PsycInfo, Web of Science, and Econlit, we found 81 studies that met these eligibility criteria. The acknowledgment and discussion of the IV conditions varied considerably. While most studies (93%) empirically verified condition (1), few studies (15%) clearly stated and discussed theoretical justifications for both conditions (2) and (3). Only 20% reported a falsification test of the IV conditions, and no study reported two or more such tests. Moreover, all studies reported a point estimate, meaning they implicitly assumed a fourth condition, while only 10% clearly stated and discussed the condition they were evoking. Causal inference relies on transparency of assumptions, but the conditions underlying IV methods are often not presented in a transparent manner. This is particularly disconcerting because even relatively small violations of the IV conditions can lead to large biases in unpredictable or counterintuitive direction. We will outline steps for the reporting of IV methods in order to help investigators present IV analyses in such a way that colleagues can better evaluate the estimates.

074

DO YOU BELIEVE IN GHOST POPULATIONS? PRESENTATION AND ILLUSTRATION OF A SIMPLE ADJUSTMENT FACTOR FOR INVERSE-PROBABILITY WEIGHTING. *Michelle Odden, Jonathan Snoweden (Oregon State University, Corvallis OR 97331)

Inverse probability weights (IPW) are frequently used to account for informative censoring and the resulting missing data. This method creates a counterfactual population in which all potential outcomes are observed. In general, IPW assigns greater weights to those persons with poor health status, who are more likely to die. This method has been criticized as creating a population of "undead" that is not realistic or relevant. Here, we present an adjustment factor for IPW to more accurately represent the experience of the study population. This factor attenuates the IPW in proportion to the amount of person-time alive divided by the potential person-time (PT_{alive} / $PT_{potential}$), for each strata with (near) equivalent probability of death. Alternatively, if time to death is not available, this factor can be estimated by the sum of the number alive and half of the number dead, divided by the total sample ($(n_{alive} + n_{dead}/2) / n_{total}$). Based on this method, we estimate potential outcomes that precede death, while allowing for mortality. We present an illustrative example based on a simulation of the association between physical activity and disability 10 years later (n = 4450), and discuss assumptions required for estimation. We assume persons who are inactive or who will develop a disability are more likely to die; therefore, the observed relative risk (RR = 0.33) is an overestimate of the true association between physical activity and disability. We use IPW to model a counterfactual population in which there is no death, and the resulting RR is 0.51. When we apply the adjustment factor to IPW to account for those participants who died, the RR is 0.46. This estimate more accurately represents the effect of physical activity in a population who may avoid disability, but still maintain a probability of dying.

075-S

CHOOSING BETWEEN INSTRUMENTAL VARIABLE ANALYSES AND CONVENTIONAL ANALYSES: THE ROLE OF SAMPLE SIZE. *Anna G C Boef, Olaf M Dekkers, Jan P Vandenbroucke, Saskia le Cessie (Leiden University Medical Centre, Leiden The Netherlands)

Instrumental variable (IV) analysis is a potentially promising tool for estimation of therapeutic effects from observational data due to its ability to circumvent unmeasured confounding. In order for an IV to be valid, strong assumptions must hold. However, even if these assumptions hold, IV analyses will not necessarily provide an effect estimate closer to the true treatment effect than conventional analyses which are unable to handle unmeasured confounding. Using simulations and calculations we investigated how effect estimates from ordinary least squares regression and two-stage least squares instrumental variable regression compare depending on sample size. The average deviation from the true effect of the estimates from the different analyses was compared. We varied sample size, instrument strength and level of unmeasured confounding. Main instrumental variable assumptions were fulfilled by design in all scenarios. Although biased, the ordinary least squares estimates were closer on average to the true effect than IV estimates at small sample sizes due to their smaller variance. Since the variance of the IV estimates decreases substantially with increasing sample size, IV estimates eventually outperformed ordinary least squares estimates at sample sizes of at least several thousands. The stronger the instrument is and the stronger the unmeasured confounding is, the smaller the sample size at which the IV estimates are closer on average to the true effect than the ordinary least squares estimates.This indicates that even when all IV assumptions hold, IV analysis can only be expected to provide a better estimate of treatment effect than conventional methods of analysis in large study populations. How large this study population should be depends on the strength of the available instrument and the expected amount of unmeasured confounding.

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WITHDRAWN

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077-S

RECURRENCE OF GESTATIONAL HYPERTENSIVE DISORDERS AND IMPACT ON NEWBORN OUTCOMES. *Nansi Boghossian, Edwina Yeung, Pauline Mendola, S. Katherine Laughon, Stephanie Hinkle, Cuilin Zhang, Paul Albert (Division of Epidemiology, Statistics, and Prevention Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Rockville MD 20892)

Preeclampsia (PE) and gestational hypertension (GH) often recur in subsequent pregnancies. How recurrence and changes in type of hypertensive disorder impact newborn outcomes is not well studied. We examined recurrence of PE, recurrence of GH, GH after PE and PE after GH in a retrospective cohort of 26,963 nulliparous women with their first 2 singleton births in Utah (2002-2010). First, we identified risk factors for recurrence by evaluating prepregnancy body mass index (BMI), interpregnancy interval, smoking, marital status, prior preterm delivery <34 weeks (PTB34) and prior small for gestational age (SGA). Second, we estimated how recurrence impacted neonatal morbidities including SGA, PTB34 and neonatal intensive care unit (NICU) admission. Poisson regression models with robust variance estimators estimated recurrence risks and newborn morbidities. Recurrence of PE, GH, PE after GH and GH after PE, occurred in 11.4%, 13.0%, 11.8% and 5.6% of women, respectively. Being overweight or obese was the most consistent risk factor of recurrence of any of the hypertensive disorders [relative risks (RRs) ranging 1.6-2.2, $p \leq 0.02$]. Additionally, PE recurrence was associated with being non-White [RR = 1.8; 95% confidence interval (CI): 1.1, 2.7] and having a prior PTB34 (RR = 2.2; 95%CI: 1.4, 3.4). Adjusting for maternal age, race, prepregnancy BMI and smoking, recurrent PE increased the risk of PTB34 (RR = 9.7; 95%CI: 4.8, 19.3) and NICU admission (RR = 1.2; 95%CI:1.0, 1.4) while PE after GH increased the risk of PTB34 (RR = 5.0; 95%CI = 1.3, 18.3) and SGA (RR = 1.9; 95%CI: 1.0, 3.5). Neither GH after PE nor recurrent GH increased newborn morbidity.

078

FOLIC ACID FORTIFICATION OF CORN MASA FLOUR AND NEURAL TUBE DEFECT PREVENTION. *Sarah Tinker, Owen Devine, Cara Mai, Heather Hamner, Jennita Reefhuis, Suzanne Gilboa, Nicole Dowling, Margaret Honein (Centers for Disease Control and Prevention, Atlanta GA 30333)

Background: Hispanics in the US have a higher prevalence of neural tube defect (NTD)-affected pregnancies than non-Hispanic whites, and lower median folic acid intake. Folic acid fortification of corn masa flour (CMF) is a policy-level intervention for NTD prevention; however, the likely impact on NTD prevalence has not been estimated. Methods: We developed a model to estimate the percentage reduction in prevalence of spina bifida and anencephaly (NTDs) that could occur with folic acid fortification of CMF. Model inputs included estimates of the percentage reduction in U.S. NTD prevalence attributed to folic acid fortification of enriched cereal grain products (ECGP) (1995-1996 vs. 1998-2002), the increase in median folic acid intake after ECGP fortification, and the estimated increase in median folic acid intake that could occur with CMF fortification at the same level as ECGP (140 μg/100g). We used Monte Carlo simulation to quantify uncertainty. We stratified analyses by racial/ethnic group and rounded results to the nearest 10. Results: We estimated CMF fortification could prevent 30 Hispanic infants from having spina bifida (95% uncertainty interval: 0, 80) and 10 infants from having anencephaly (95% uncertainty interval: 0, 40) annually. The estimated impact among non-Hispanic whites and blacks was smaller. Discussion: CMF fortification with folic acid could prevent from 0 to 120 infants, with the most likely value of approximately 40, from having spina bifida or anencephaly among Hispanics, the population most likely to benefit from the proposed intervention. While potentially meaningful, this estimated reduction is unlikely to be discernible using current birth defect surveillance methods.

079

AGE AT MENARCHE AND ITS RELATIONSHIP TO BODY MASS INDEX AMONG ADOLESCENT GIRLS IN KUWAIT. *Abdullah Al-Taiar, Nora Al-Awadhi, Nouf Al-Kandari, Teebah Al-Hasan, Daliah AlMurjan, Salhah Ali (Faculty of Medicine, Kuwait University, Kuwait Kuwait)

Background: Despite the increasing rates of childhood obesity and rapid change in socio-economic status, the mean age at menarche remains mostly unknown among contemporary girls in Kuwait and other countries in the Gulf region. This study aimed to estimate the mean age at menarche among schoolgirls in Kuwait and investigate the association between age at menarche and obesity. Methods: A cross-sectional study was conducted on 1,273 randomly selected female high school students from all governorates in Kuwait. Overweight was defined as higher than or equal to the 85th percentile and obesity as higher than or equal to the 95th percentile. Data on menarche, socio-demographic status, physical activity and diet were collected using confidential self-administered questionnaire. Results: Out of 1,273 students, 23 (1.8%) were absent or refused to participate. The mean (SD) age at menarche was 12.41 (1.24) years (95% CI: 12.35-12.48). The prevalence of early menarche, defined as less than 11 years of age, was 8.5% (95% CI: 7.0-10.2). The prevalence of obesity and overweight was 18.3% (95% CI: 16.2-20.6%) and 25.8% (95% CI: 23.42-28.30%), respectively. Early age at menarche was significantly associated with overweight and obesity before and after adjusting for potential confounders. Conclusion: Age at menarche among contemporary girls in Kuwait is similar to that in industrialized countries. There is an inverse association between age at menarche and obesity or overweight. Trends in menarcheal age should be monitored and taken into account in strategies that aim to combat obesity.

080

COMPARISON OF PROSPECTIVE AND RETROSPECTIVE MEASUREMENTS OF FREQUENCY OF SEXUAL INTERCOURSE. *Larissa Brunner Huber, Jordan Lyerly, Ashley Young, Jacek Dmochowski, Tara Vick, Delia Scholes (University of North Carolina, Charlotte NC 29223)

Objective: Measurements of sexual intercourse frequency have been acknowledged as informative for research on pregnancy, contraception, and sexually transmitted infections, however, collecting data on this sensitive topic is complex. The purpose of this study was to determine whether retrospective recall of sexual intercourse frequency is consistent with information obtained through the use of prospective daily diary methods in a diverse sample of women. Methods: A total of 98 women who participated in the Fertility and Oral Contraceptive Use Study completed baseline interviews and provided complete information on sexual intercourse frequency on diaries (prospective) and postcards (retrospective). Linear mixed models were used to test for variation in response within categories of demographic and other variables. Results: The mean number of days women had sexual intercourse per week was 1.5 day using prospective diary information versus 2.0 days when using 3-month retrospective recall ($p < 0.001$). Mean differences for the various sociodemographic subgroups were positive for all groups indicating that women consistently reported a higher frequency of sexual intercourse on the retrospective postcards than they recorded on their prospective diaries; however, these mean differences did not vary significantly. Conclusions: If confirmed in other samples, the use of retrospective methods may be adequate to accurately collect data on sexual intercourse frequency—and may be preferable. Using only one retrospective measurement could decrease study costs, the burden to participants, and have a higher response rate.

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081-S

MATERNAL OBESE, VITAMIN D STATUS AND RISK OF PREECLAMPSIA. *Shu Qin Wei, Zhong-Cheng Luo, William Fraser (CHU Sainte Justine, Montreal QC Canada)

Objective: To examine the associations between maternal plasma levels of 25-hydroxyvitamin D [25(OH)D] and pre-pregnancy body mass index (BMI) and the risk of preeclampsia. Study design: This is a prospective cohort study of 697 pregnant women. Maternal plasma 25(OH)D levels were measured at 12-18 weeks and 24-26 weeks of gestation using chemiluminescence immunoassay. Results: In all, 18% of pregnant women were obese (BMI $\geq$ 30). Forty percent had plasma 25(OH)D levels less than 50nmol/l. Maternal plasma 25(OH)D levels at 12-18 weeks and 24-26 weeks gestation gestation were inversely associated with pre-pregnancy BMI (at 12-18 weeks gestation: r = -0.223, p <.0001; at 24-26 weeks gestation: r = -0.182, p < .0001; respectively). Compared to non-obese women, obese women had higher prevalent rate of low vitamin D status [25(OH)D less than 50 nmol/L] (at 12-18 weeks gestation: 54.2% vs. 35.0%, p < .0001; at 24-26 weeks gestation :50.9% vs.34.3%, p = .0001; respectively). Pregnant women who developed preeclampsia had higher mean BMI compared those who did not (mean BMI: 28.0-7.0, 25.6 vs. 25.1-5.6, 23.5, p = 0.02). Interestingly, non-obese women with 25(OH)D < 50 nmol/L at 24-26 weeks gestation experienced a marked increase in the risk of preeclampsia (aOR 4.33, 95% CI 1.53-12.24). However, for obese women, there was no statistical evidence of such an association (aOR 1.63, 95% CI 0.35-7.57). Conclusion: Maternal obesity is associated with an increased prevalence of vitamin D deficiency during pregnancy. The association between maternal low vitamin D status during pregnancy and preeclampsia was only in non-obese women. Keywords 25-hydroxyvitamin D, obesity, preeclampsia

082-S

MATERNAL VITAMIN D RECEPTOR GENE POLYMORPHISMS, VITAMIN D STATUS IN PREGNANCY AND PRETERM BIRTH RISK. *Shu Qin Wei, William Fraser (CHU Sainte Justine, Montreal QC Canada)

Objective: Vitamin D is a known immune system modulator and has been shown associated with inflammatory response. Vitamin D's effects are exerted via the vitamin D receptor (VDR) and there is VDR genetic variation in the population. However, there is lack of evidence on how the maternal vitamin D status interact with the VDR gene single nucleotide polymorphisms (SNPs) and risk of spontaneous preterm birth. The aim of this study was to determine the relationships among maternal vitamin D receptor polymorphisms, vitamin D status in pregnancy and risk of preterm birth. Study Design: This is a prospective cohort study of 697 pregnant women. Maternal plasma 25(OH)D at 12-18 weeks gestation were measured using chemiluminescence immunoassay. Polymerase chain reaction/restriction fragment length polymorphism was applied to test the genotype frequency of vitamin D receptor gene polymorphisms [ApaI (rs7975232), BsmI (rs1544410), Cd × 2 (rs11568820), FokI (rs2228570), TaqI (rs731236) and Tru91 (rs757343)]. Results: Maternal vitamin D receptor gene BsmI and TaqI polymorphisms were associated with low vitamin D status [25(OH)D less than 50 nmol/L] (both p < .005). The frequency of BsmI GG + AG genotype, TaqI TT + CT genotype were significantly higher in women who developed preterm birth compared with those who did not (24.0% vs. 14.1%, P = 0.01; 22.7% vs. 14.5%, P = 0.04; respectively). The vitamin D receptor gene ApaI, Cd × 2, FokI, and Tru91 polymorphisms did not show any difference in patients who developed preterm birth compared with those who did not (P >0.05). After adjusting for potential confounding factors, logistic regression analysis showed that both BsmI GG + AG and TaqI TT + CT genotype were associated with an increased risk or preterm birth (aOR 3.09, 95% CI 1.14 - 8.43; aOR 3.06, 95%CI 1.08-8.67) in only women with low vitamin D status [25(OH)D < 50 nmol/L]. Conclusion: Our findings suggest that maternal vitamin D receptor gene BsmI and TaqI polymorphism may be associated with risk of preterm birth in pregnant women with low vitamin D status.

083-S

SEASONAL VARIATION OF TOTAL 25-HYDROXYVITAMIN-D IN A POOLED SAMPLE OF BLACK AND WHITE PREGNANT WOMEN FROM THREE US PREGNANCY COHORTS. *Miguel-Angel Luque-Fernandez, Bizu Gelaye, Tyler Vander Weele, Cynthia Ferre, Anna Maria Siega-Riz, Claudia Holzman, Daniel Enquobahrie, Nancy Dole, Michelle A Williams (Harvard School of Public Health, Boston, MA 02115)

Background: Serum concentration of total 25-hydroxyvitamin-D (25OHD) varies within individuals and across populations seasonally. We evaluated seasonal variation of 25OHD (25OHD3 and 25OHD2) among pregnant women, focusing on pattern and determinants of variation. Methods: 2,583 non-Hispanic Black and White pregnant women in a multi-center case-control study nested within three cohorts had antenatal 25OHD concentrations determined using mass spectrometry. Fourier time series analysis and generalized linear models were used to confirm and estimate magnitude of 25OHD seasonal variation. We modeled seasonal variability of 25OHD using a stationary cosinor model to estimate the phase shift, peak-trough difference (PTΔ), and annual mean (AM). We repeated analyses for 25OHD3 and 25OHD2 and by race and study site. Results: We observed a seasonal pattern for 25OHD, with a peak in summer, a nadir in winter, and a phase of 8 months, when the seasonal increase is symmetric to the decrease. The pattern was due to fluctuations in 25OHD3 with no evidence of seasonal variation in 25OHD2. After adjustment for study site, maternal age, and gestational age at sample collection, the AM concentrations and the estimated PTΔ of 25OHD among Black women were 19.6 (95% confidence interval [CI]: 18.9-20.4), and 5.9 (95%CI: 4.9-7.0 ng/mL), and 33.0 (95%CI: 32.6-33.5) and 7.1 (95%CI: 5.6-8.6 ng/mL) for White women. Seasonality in 25OHD varied by maternal educational attainment and pre-pregnancy obesity, but not study site. Discussion: Seasonal variability 25OHD among pregnant women was observed. Black women had lower 25OHD concentrations throughout the year and lower levels of seasonal variation than Whites.

084

SLEEP DISORDERS AND DIABETES IN PREGNANT AND NON-PREGNANT WOMEN OF CHILDBEARING AGE. *Xu Xiong, Yiqiong Xie, Pierre Buekens (Tulane University School of Public Health and Tropical Medicine, New Orleans LA 70112)

Literature suggests an association between sleep disorders and diabetes mellitus. The authors sought to examine the association between sleep disorders and diabetes in pregnant and non-pregnant women. We conducted a secondary analysis based on self-reported health and sleep characteristics collected by the National Health and Nutrition Examination Survey (NHANES) from 2005 to 2010. The present study sample included 507 pregnant women and 3,875 non-pregnant women aged 15-44 years. Univariate and multivariate logistic analyses were performed to examine the association between sleep disorders and diabetes and to adjust for age, ethnicity, smoking, body mass index, and other confounding variables. The overall prevalence of having trouble sleeping, sleep disorders (e.g., sleep apnea and insomnia), and daily sleep <7 hours was 23.5%, 7.0%, and 29.0% in pregnant women; and 21.9%, 6.7%, and 37.7% in non-pregnant women. In pregnant women, women who had trouble sleeping and daily sleep <7 hours were not at increased risk of having diabetes, with adjusted odds ratio (aOR) of 0.3 [95% confidence interval (CI): 0.1-0.9] and 0.3 (0.1-1.3). In non-pregnant women, women who had trouble sleeping, sleep disorders, and daily sleep <7 hours were also not at increased risk of having diabetes, with aOR of 1.2 (0.8-1.9), 1.7 (0.8-3.3), and 1.0 (0.7-1.3), respectively. The authors conclude that sleep disorders are not associated with an increased risk of diabetes in women of childbearing age.

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SLEEP DISORDERS AND HYPERTENSION IN PREGNANT AND NON-PREGNANT WOMEN OF CHILDBEARING AGE. *Xu Xiong, Yiqiong Xie, Pierre Buekens (Tulane University School of Public Health and Tropical Medicine, New Orleans LA 70112)

The authors sought to examine the association between sleep disorders and hypertension in pregnant and non-pregnant women. We conducted a secondary analysis based on self-reported health and sleep characteristics collected by the National Health and Nutrition Examination Survey (NHANES) from 2005 to 2010. The present study sample included 507 pregnant women and 3,875 non-pregnant women aged 15-44 years. Univariate and multivariate logistic analyses were performed to examine the association between sleep disorders and hypertension and to adjust for age, ethnicity, smoking, body mass index, and other confounding variables. The overall prevalence of having trouble sleeping, sleep disorders (e.g., sleep apnea and insomnia), and daily sleep <7 hours was 23.5%, 7.0%, and 29.0% in pregnant women; and 21.9%, 6.7%, and 37.7% in non-pregnant women. In pregnant women, women who had trouble sleeping, sleep disorders, and daily sleep <7 hours were at increased risk of having hypertension, with adjusted odds ratio (aOR) of 2.5 [95% confidence interval (CI): 1.0-6.3], 4.6 (1.4-14.7), and 1.09 (0.5-2.5), respectively. In non-pregnant women, women who had trouble sleeping, sleep disorders, and daily sleep <7 hours were also at increased risk of having hypertension, with aOR of 2.9 (2.2-3.8), 4.1 (2.5-6.7), and 1.6 (1.2-1.9), respectively. The authors conclude that sleep disorders are associated with an increasd risk of hypternsion in both pregnant and non-pregnant women of childbearing age.

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PRE-PREGNANCY BODY MASS INDEX, GESTATIONAL WEIGHT GAIN AND DEPRESSION AMONG PREGNANT HISPANIC WOMEN. Karen A. Ertel, *Marushka L. Silveira, Penelope S. Pekow, Glenn Markenson, Nancy Dole, Lisa Chasan-Taber (University of Massachusetts Amherst, Amherst MA 01003)

Research has demonstrated a positive association between obesity and depression. However, studies examining this association among pregnant women are sparse and predominantly in non-Hispanic women. We examined the relation between pre-pregnancy body mass index (BMI) and prenatal depression, and tested if gestational weight gain (GWG) modified this association among 1090 pregnant Hispanic women from Proyecto Buena Salud (2006-2011), a prospective cohort study conducted in Massachusetts. The Edinburgh Postnatal Depression Scale was administered during early (mean = 12.3 weeks gestation), mid- (mean = 21.3 weeks gestation), and late (mean = 30.6 weeks gestation) pregnancy. Scores ≥15 were considered probable major depression and ≥13 were considered at least minor depression. Information on pre-pregnancy BMI (kg/m2) and GWG were abstracted from medical records. We used longitudinal, generalized linear mixed effects models to calculate the association between pre-pregnancy BMI and depression across pregnancy. Approximately 45% of women were overweight or obese prior to pregnancy, 24% reported major depression, and 33% reported minor depression at one or more times during pregnancy. Women who were overweight (25- < 30 kg/m2) were less likely to experience probable major depression (Odds Ratio (OR) = 0.51; 95% Confidence Interval (CI) 0.28-0.91) and minor depression across pregnancy (OR = 0.53, 95% CI 0.31-0.90) as compared to normal weight women, when adjusted for sociodemographic and acculturation factors. Obese women (≥30 kg/m2), and underweight women (<18.5 kg/m2) did not have an increased risk of depression. GWG did not modify the effect of BMI on depression. Findings suggest an inverse association between overweight and risk of depression during pregnancy in this sample of predominantly Puerto Rican women.

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COLD TEMPERATURE DURING PREGNANCY AND BIRTH OUTCOMES IN UPPSALA, SWEDEN, 1915 TO 1929. *Tim Bruckner, Bitte Modin, Denny Vagero (University of California, Irvine, Irvine CA 92697)

The literature reports adverse birth outcomes following ambient heat. Less work focuses on birth outcomes following cold, and we know of no studies of cold that examine stillbirth. We test the relation between cold ambient temperature during pregnancy in Sweden and four outcomes: stillbirth, preterm, birthweight for gestational age, and birth length for gestational age (a measure of leanness). We examine births from 1915 to 1929 in Uppsala, Sweden which—unlike most societies today—experienced sub-standard indoor-heating and fewer amenities to provide shelter from cold. We retrieved data on almost 14,000 deliveries from the Uppsala Birth Cohort Study. We linked a validated, daily ambient temperature series to all pregnancies. We applied Cox proportional hazards for time-to-event outcomes (stillbirth and preterm) and linear regression for birthweight and birth length-for–gestational-age. Month indicator variables controlled for confounding by season of birth. The risk of both stillbirth and preterm rises as ambient temperature during pregnancy falls (hazard ratio [HR] of stillbirth for a 1.0°C fall in temperature = 1.09; 95% Confidence Interval [CI]: 1.01 — 1.18; HR of preterm for a 1.0°C fall in temperature = 1.05; 95% CI: 1.01 — 1.10). Colder ambient temperatures during pregnancy also predict more lean (i.e., thinner) infants. We, however, observe no relation between cold and birthweight for gestational age. In historical Sweden, cold temperatures during pregnancy increase the risk of stillbirth and other adverse outcomes. Our work holds relevance to maternal-fetal biology as well as to contemporary societies (e.g., indigenous Arctic populations) with limited resources to mitigate the adverse consequences of cold.

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NEONATAL HEALTH OF INFANTS BORN TO MOTHERS WITH ASTHMA. *Pauline Mendola, Tuija I Mannisto, Kira Leishear, Uma M Reddy, Zhen Chen, S. Katherine Laughon (Eunice Kennedy Shriver National Institute for Child Health and Human Development, Rockville MD 20852)

Women with asthma have increased risk for obstetric complications, preterm birth (PTB) and fetal growth restriction. We examined neonatal complications among singleton infants (n = 223,512) in the Consortium on Safe Labor (2002-2008), a retrospective nationwide US cohort of deliveries at 23 weeks gestation or greater. Infants born to mothers with asthma (n = 17,044) were compared to newborns of non-asthmatic women using regression models with generalized estimating equations to calculate adjusted odds ratios (OR) and 95% confidence limits (CI) adjusting for site, maternal age, race, marital status, insurance, pre-pregnancy body mass index, smoking, alcohol, chronic disease, parity and cesarean delivery. Outcomes including gestational age, birth weight, mortality, resuscitation at delivery, neonatal intensive care unit (NICU) admission, respiratory distress syndrome, apnea, sepsis, anemia, transient tachypnea, infective pneumonia, asphyxia, intracerebral hemorrhage, seizure, cardiomyopathy, peri- or intraventricular hemorrhage, necrotizing enterocolitis, aspiration and retinopathy of prematurity were derived from electronic medical records. Analyses by gestational week indicated significantly increased risk of PTB beginning at 33 weeks for women with asthma. The odds of being small for gestational age (SGA) were increased (OR = 1.11, CI: 1.05-1.16) and NICU admissions were more common when mothers had asthma (OR = 1.15, CI: 1.10-1.20) as were cases of respiratory distress syndrome (OR = 1.13; CI: 1.04-1.23), transient tachypnea (OR = 1.13, CI: 1.05-1.22), and asphyxia (OR = 1.39, CI: 1.07-1.81) but no other complications. Analyses restricted to term infants yielded similar results with additional risk for intracerebral hemorrhage (OR = 1.84, CI: 1.11-3.03) and anemia (OR = 1.30, CI: 1.04-1.62). In addition to anticipated increases in PTB and SGA, respiratory morbidity and NICU admission appear to be increased in neonates of women with asthma.

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ASSOCIATIONS OF DIET AND PHYSICAL ACTIVITY WITH THE 3 COMPONENTS OF GESTATIONAL WEIGHT GAIN. *Xiaozhong Wen, Faye Justicia-Linde, Kailing Kong, Caixia Zhang, Weiqing Chen, Leonard Epstein, Sheryl Rifas-Shiman, Matthew Gillman (State University of New York, Buffalo NY 14214)

Objective: To examine effects of diet and physical activity (PA) on the 3 components (fetus, placenta, and maternal weight gain) of gestational weight gain (GWG). Methods: We analyzed a sub-sample (N = 852) of Project Viva, a pre-birth cohort in Massachusetts. Pregnant women self-reported their diet at 1st (Tri1) and 2nd trimester (Tri2) and physical activity at Tri2. We calculated maternal weight gain by subtracting measured fetal and placental weight at delivery from total GWG. We fitted multivariable linear regression models for internal z-scores of 3 GWG components, adjusting for maternal age, race/ethnicity, parity, prepregnancy body mass index, energy intake (for nutrients), and the child sex and gestational age. Results:Tri2 energy intake was positively associated with maternal weight gain (mean difference in weight z-score per 500 kcal/day increment in energy intake, 0.11 [95% confidence interval, 0.05 to 0.17]) but not with fetal or placental weight, whereas Tri2 PA (-0.29 [-0.43,-0.15] per 10 minutes/day) was inversely associated. The percentage of energy from protein during Tri1 (0.15 [0.02,0.28] per 10 percent) and polyunsaturated fat during Tri2 (0.25 [0.01,0.49]) were positively associated with maternal weight gain, but that from other fatty acids or carbohydrates was not associated. Vegetarian diet during Tri2 was associated with lower fetal (-0.39 [-0.71,-0.08]) and placental weight (-0.40 [-0.79,-0.01]), but not with maternal weight gain. Conclusion: In our sample, lower energy intake and higher PA during mid-pregnancy might reduce maternal weight gain without impacting fetal and placental weight. In contrast, vegetarian diet during mid-pregnancy seems to specifically restrict fetal and placental growth.

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FATHERS MATTER: THE ROLE OF PATERNAL AGE IN INFANT MORTALITY. *Lauren Doamekpor, Ndidiamaka Amutah, Lauren Ramos (University of Maryland College Park, Department of Family Science, College Park MD 20742)

Background: Correlates of age and health are vital to research on infant and birth outcomes. The literature highlights that infant death varies by maternal age, with young and older women at higher risk. The link between paternal age and birth outcomes has received little attention. This study seeks to examine the added impact of paternal age on infant mortality, above and beyond that of maternal age among married couples, as well as the influence of prenatal care in mediating risks. A limited number of studies suggest that paternal age is associated with negative birth outcomes, and various high case-fatality diseases. Methods: Using the 2002 linked birth and infant death dataset (N = 63,754), hazard ratios for the association between combined younger (<20 years old) and older maternal (>21 years and older) and paternal age and the risk of infant mortality were estimated. Data with missing information were removed from the study. Maternal demographic characteristics, such as education, and race/ethnicity were controlled. Results: The key findings indicate that, independent of maternal education and race/ethnicity, young paternal age adds additional risk, above and beyond that of maternal age, only when the mother is older (HR = 2.7, $p < 0.05$,). Compared to couples that were both older, couples where the mother was older, and the father was younger had the highest risk of infant mortality, which was statistically significant. Conclusions: Although paternal age has an effect on birth outcomes independently, to our knowledge, this is the first study to examine male age related disparities and pregnancy outcomes using both maternal and paternal age variables. This study highlights the importance of young paternal age as a significant factor in the risk of infant death, however, more research is needed to further develop the understanding of the relationship between paternal age and infant mortality.

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PREGNANCY COMPLICATIONS AMONG WOMEN OIF/OEF VETERANS. *Jodie Katon, Kristin Mattocks, Gayle Reiber, Elizabeth Yano, Lisa Callegari, Eleanor Schwarz, Laurie Zephyrin, Joseph Goulet, Sally Haskell, Cynthia Brandt (Department of Veterans Affairs Puget Sound Health Care System, Seattle WA 98108)

Introduction: Compared with non-Veterans, women Veterans may be at increased risk of gestational diabetes (GDM) and preeclampsia, which are risk factors for type 2 diabetes and cardiovascular disease. Lifestyle intervention can reduce these risks. Objective: To describe the prevalence of GDM and preeclampsia among women Veterans from Operation Iraqi Freedom and Operation Enduring Freedom (OIF/OEF) whose delivery was paid for by VA, and determine whether complications of pregnancy are associated with return to VA in the year following delivery. Methods: Women OIF/OEF Veterans whose delivery was paid for by VA were identified through linkage with the OIF/OEF roster and use of diagnostic related group codes. Complications of pregnancy were identified by presence of ICD-9 codes in the inpatient or outpatient files in the nine months preceding the delivery for gestational diabetes, gestational hypertension, or preeclampsia/eclampsia. Return to VA in the year following delivery was defined as receipt of any VA care in the 365 days following delivery. We estimated the association of complications of pregnancy with return to VA in the year following delivery using Cox proportional hazards regression. Results: We identified 2,223 deliveries among women OIF/OEF Veterans paid for by VA. 70% of these women Veterans were 18-25 years old. In total 5% had GDM, 3.9% had gestational hypertension, and 5.9% had preeclampsia/eclampsia. After adjustment, presence of GDM, gestational hypertension, or preeclampsia/eclampsia was not associated with increased likelihood of return to VA in the year following delivery (hazard ratio 1.05; 95% confidence interval 0.92, 1.20). Conclusion: Women OIF/OEF Veterans have a high risk of complications of pregnancy similarly aged non-Veteran women. Ensuring that these women Veterans return to VA following delivery for appropriate follow-up such as lifestyle intervention is crucial to prevent development of chronic diseases.

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BODY MASS INDEX AND PHYSICAL ACTIVITY ARE NOT ASSOCIATED WITH SPERM MORPHOLOGY, MOTILITY AND CONCENTRATION IN ADULT SON'S IN THE CHILD HEALTH AND DEVELOPMENT STUDIES. *Elizabeth Widen, Piera Cirillo, Barbara Cohn, Linda Kahn, Xinhua Liu, Pam Factor-Litvak (Columbia University, New York NY 10003)

There is mixed evidence regarding the relationship between body mass index (BMI) and sperm quality. Further, it is not known whether physical activity is associated with semen quality. Here we report on the relationships between current/previous BMI and physical activity on semen quality in men ages 38-47 years. Subjects were a subgroup of male offspring of the Child Health and Development Studies, a pregnancy cohort enrolled between 1959 and 1967 at the Kaiser Foundation Health Plan in the Oakland, California area. In 2005, adult sons (n = 338) participated in a follow-up study. Semen samples (n = 196) were analyzed for sperm concentration, motility and morphology. Current physical activity and weight history for ages 20-29 were obtained by self-report. Regression was used to examine the relationship between BMI, physical activity and semen outcomes, adjusting for age, race, smoking, and time since last ejaculation. Mean sperm concentration was 72.5 million sperm per ml of ejaculate (Standard deviation (SD): 59.1), mean percent motile was 47.0% (SD: 17.6%) and mean percent with normal morphology was 7.6% (SD: 4.2%). Mean current BMI was 28.6 kg/m2 (SD: 5.5 kg/m2), while mean BMI in 20's was 24.2 kg/m2 (SD: 3.45 kg/m2). Current/previous BMI and physical activity were not significantly associated with sperm parameters, however there were non-significant trends between higher current/previous BMI and lower percent motility and concentration [Estimated motility β: -0.23 (95% Confidence Interval (CI): -0.69, 0.22); -0.38 (95% CI: -1.13, 0.37); Estimated concentration β: -0.02 (95% CI: -0.05, 0.01); -0.03 (95% CI: -0.08, 0.03)] for current and previous BMI respectively. In this sample of middle age men, these findings suggest no association between BMI and semen morphology or physical activity. While trends were observed between higher current/previous BMI and lower semen motility and concentration, larger sample sizes may be needed to detect associations.

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BORN INFORMATION SYSTEM REPORTING FOR ONTARIO HEALTHCARE ORGANIZATIONS. *Sherrie Kelly, Barbara Chapman, Sandra Dunn, Ann Sprague, Monica Prince, Mari Teitelbaum (BORN Ontario, Ottawa ON Canada)

Objectives: 1) To implement a maternal-child reporting system across Ontario for healthcare providers, administrators, and decision and policy makers to have access to data across the continuum of care. 2) To compare hospital performance results using the Maternal Newborn Dashboard reporting tool to assess the beneficial impact on clinical best practices. Approach: In 2012, BORN (Better Outcomes Registry & Network) Ontario launched the BORN Information System (BIS) in 106 hospitals, 82 midwifery practice groups (MPGs), and prenatal and newborn screening labs across Ontario, Canada. Three reporting modules were created: administrative reports for data quality management, clinical reports for access to clinical indicator data, and analytical reports for customized data queries. The Maternal Newborn Dashboard, an audit and feedback clinical reporting tool with six key performance indicators (KPIs), benchmarks, and comparator data, was recently launched for all hospitals. A linear regression analysis of repeated monthly and quarterly rates is underway to trend BORN KPI data. Results: Ontario has approximately 40% of Canadian births and now has real-time data access across the continuum of care (prenatal screening, antenatal care, labour and birth, and newborn screening) for all maternal-newborn hospitals and MPGs. Users can compare their data with other similar level of care and birth volume hospitals, health regions, and provincial data. Missing data and confidence intervals (95% CI) are reported where appropriate. Preliminary Maternal Newborn Dashboard report results from a pilot study in 10 Eastern Ontario region hospitals showed an overall 41.3% decrease in the rate of elective repeat cesarean section prior to 39 weeks' gestation (one of the six KPIs) using data from 2009-10 to 2011-12. Conclusion: The novel real-time BIS online reporting modules provide data to users and system planners to support clinical best practice, quality improvement, and development of health policy. We have started to evaluate performance across Ontario with the ultimate goal of adding value and improving the quality of care within the maternal-child health system.

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EXPOSURE TO ENVIRONMENTAL CHEMICALS DURING PREGNANCY AND FETAL MARKERS OF METABOLIC DYSFUNCTION. *Linda Dodds, Tye Arbuckle, Adrienne Etinger, Jillian Ashley-Martin, Mandy Fisher, Shayne Taback, Erin Keeley, Maryse Bouchard, Patricia Monnier, Renee Dallaire, William Fraser (Dalhousie University, Halifax NS Canada)

Obesity and type-2 diabetes are on the rise and in-utero exposure to environmental contaminants is suspected to play a role, although data are sparse. This study used data from Maternal Infant Research on Environmental Chemicals Study (MIREC), a cohort of 2001 women recruited during the first trimester of pregnancy from 10 Canadian sites to examine associations between exposure to environmental chemicals during early pregnancy and markers of fetal metabolic dysfunction. Environmental contaminants, including metals, phthalates, brominated flame retardants, bisphenol A, etc., were measured in maternal blood or urine. Leptin and adioponectin levels were measured in cord blood and served as markers of metabolic dysfunction. Covariates, such as maternal body mass index and age, were assessed as potential confounders and effect modification by sex was assessed. Adjusted logistic regression models were used to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between environmental chemicals and fetal levels of leptin or adioponectin. There were 1,981 women who had a live birth and a first trimester blood or urine sample available. Of these, there were 1,362 with a cord blood sample. Leptin levels were significantly higher in females than males, but adiponectin levels did not differ by sex. Monoethyl phthalate was associated with elevated leptin level (top 10th percentile) only in males (adjusted OR = 1.88, 95% CI = 1.01-3.50). Among metals, maternal lead and cadmium levels were significantly associated with elevated leptin level in males. No associations were found between the environmental chemicals investigated and cord blood adiponectin level, overall. Prenatal exposure to certain environmental chemicals may be associated with markers of fetal metal dysfunction in a sex-dependent fashion. Long-term implications for metabolic status and the risk of obesity should be investigated further.

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COMPARABILITY OF MATERNAL RISK FACTORS BETWEEN MOTHERS WITH GEOCODED AND UNGEOCODED ADDRESSES. J Brender, *M Shinde, F Zhan, P Langlois (Texas A&M Health Science Center, College Station TX 77843)

In studies of residential proximity to pollution sources and adverse pregnancy outcomes, a proportion of maternal residential addresses will lack sufficient information to assign exposure status. Very little information exists regarding the comparability of other risk factors among births between mothers with geocoded and ungeocoded addresses. In a case-control study of residential exposure to air pollutants and birth defects that utilizes information from vital records for 1996-2008 Texas births, we compared the strength of associations between maternal race/ethnicity, education, and smoking and selected birth defects. The study population included 305,540 mothers with addresses coded to street level and 36,923 mothers with ungeocoded addresses. Most associations between maternal characteristics and birth defects were similar between mothers with geocoded and ungeocoded addresses. However, relative to more than 12 years education, less than 12 years of education among mothers with geocoded addresses was associated with births with spina bifida (odd ratio (OR) 1.4, 95% confidence interval (CI) 1.1, 1.8), while this association was absent among mothers with ungeocoded addresses (OR 1.0; 95% CI 0.53, 2.0). Compared to non-Hispanic white mothers, Hispanic ethnicity was positively associated with anencephaly in the geocoded group (OR 1.4; 95% CI 1.1, 1.7), but negatively associated with anencephaly in the ungeocoded group (OR 0.73; 95% CI 0.57, 0.94). Smoking was more strongly associated with oral clefts in the ungeocoded (OR 2.0; 95% CI 1.4, 2.8) than geocoded group (OR 1.4; 95% CI 1.2, 1.6). Overall, the associations between maternal characteristics and several types of birth defects were similar by geocoded status with a few notable exceptions.

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THE ASSOCIATION BETWEEN PARITY AND BIRTHWEIGHT IN A LONGITUDINAL CONSECUTIVE PREGNANCY COHORT. *Stefanie Hinkle, S Katherine Laughon, Lindsey Sjaarda, Pauline Mendola, Nansi Boghossian, Edwina Yeung, Paul Albert (Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda MD 20892)

Nulliparity has been associated with lower birthweight; however, prior studies were mostly cross-sectional, capturing nulliparous women who may not have other children and therefore not fully comparable to multiparous women. Furthermore, studies have not adequately accounted for important confounders that influence birth weight. We used longitudinal medical data from a retrospective hospital-based cohort of 39,579 women with two to six singleton deliveries >37 weeks, from 2002-2010 in Utah. Using nulliparous women as the reference, we calculated sex and gestational age specific birthweight z-scores. The association between parity and birthweight z-score was examined using linear mixed models with a random effect by woman and parity estimated using a piecewise function with a single term estimating the change between 0 and 1 and linear term when parity >1. All models were adjusted for pregnancy specific variables including maternal prepregnancy body mass index (BMI), gestational weight gain (GWG), sociodemographics, smoking and alcohol use, chronic diseases, and pregnancy complications. Among nulliparous women, mean (standard deviation) prepregnancy BMI, GWG, and birthweight z-score were 23.8 (4.8) kg/m2, 15.2 (5.8) kg, and 0.00 (1.0), compared to 24.5 (5.4) kg/m2, 13.6 (5.7) kg, and 0.21 (1.00) among primiparous women, respectively. Using longitudinal adjusted models, offspring birthweight increased by 0.19 (95% confidence interval (CI): 0.17, 0.20) z-score units from parity 0 to 1 and by 0.04 z-score units (95% CI: 0.03, 0.05) per unit increase in parity >1. Parity is independently associated with birthweight, with the greatest increase observed between first and second born infants of the same mother.

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MATERNAL EXPOSURE TO CHILDHOOD ABUSE IS ASSOCIATED WITH ELEVATED RISK OF AUTISM. *Andrea Roberts, Kristen Lyall, Janet Rich-Edwards, Alberto Ascherio, Marc Weisskopf (Harvard School of Public Health, Boston MA 02115)

Context: Adverse perinatal circumstances have been associated with increased risk of autism. Women exposed to childhood abuse experience more adverse perinatal circumstances than women unexposed, but whether abuse is associated with autism in offspring is unknown. Methods: We examined whether maternal exposure to childhood abuse is associated with risk of autism, and whether possible increased risk is accounted for by higher prevalence of adverse perinatal circumstances among abused women, including gestational diabetes, toxemia, intimate partner abuse, prior abortion, preterm delivery, low birth weight, alcohol use, and smoking, in a longitudinal cohort (N mothers of children with autism = 451; N mothers of children without autism = 52,498). Autism spectrum disorder was assessed by maternal report, validated with the Autism Diagnostic Interview-Revised in a subsample. Results: Exposure to abuse was associated with increased risk of autism in children in a monotonically increasing fashion. The highest level of abuse was associated with the greatest prevalence of autism (1.8% versus 0.7% in women not abused, P = 0.005) and the greatest risk for autism adjusted for demographic factors (risk ratio = 3.7, 95% confidence interval = 2.3, 5.8). All adverse perinatal circumstances were more prevalent in women abused except low birth weight. Adjusted for perinatal factors, the association of maternal abuse with autism was slightly attenuated (highest level of abuse, risk ratio = 3.0, 95% confidence interval = 1.9, 4.9). Conclusions: We identify an intergenerational association between childhood exposure to abuse and risk for autism in the subsequent generation. Adverse perinatal circumstances accounted for only a small portion of this increased risk.

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PSYCHOLOGICAL DISTRESS IN THE NATIONAL HEALTH INTERVIEW SURVEY (NHIS) AND MEDICARE HOSPITALIZATIONS. *Hannah R Day, Laura A Pratt, Julie A Weeks, Jennifer D Parker (Centers for Disease Control and Prevention, Hyattsville MD 20782)

Depression and other instances of psychological distress at an index hospitalization are associated with readmissions. Few studies have the capability to combine community based mental health measures with hospitalization records. The National Health Interview Survey-Medicare linkage provides a unique opportunity to study data obtained from survey participants with longitudinal outcomes recorded in administrative data. We conducted a prospective cohort study of adults age 65 and over who participated in the NHIS from 1997-2005 with data linked to Medicare a year later (1998-2006) to determine the association between serious psychological distress in the community and hospitalization one year later. Serious psychological distress was measured in the community using the Kessler 6 at the time of NHIS data collection, and the outcome of hospitalization was obtained through linked administrative records. Univariate, bivariate and logistic regression analyses were completed in SAS callable SUDAAN version 11.0.0. 285,468 linked sample adults provided data on the Kessler 6. Serious psychological distress (n = 9,964) was more common in females, smokers, widows, adults with four or more comorbidities and adults with lower levels of education. 9,726 adults were hospitalized the year after their NHIS survey year. Adjusting for age, sex and education, race, smoking, marital status and number of self-reported conditions, adults with serious psychological distress in the community were 1.4 times more likely to have hospital admissions (OR: 1.4; 95% Confidence Interval 1.2-1.6). Sensitivity analyses show odds ratios were similar for one hospitalization or more than one. Older adults with high levels of psychological distress in the community may be at increased risk of future hospitalizations.

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EXPOSURE TO TRAUMATIC EVENTS AND CHANGES IN DEPRESSION SEVERITY IN AN URBAN AREA. *Melissa Tracy, Kara Zivin, Hal Morgenstern, Sandro Galea (Columbia University, New York NY 10032)

The relation between traumatic event experiences and depression is well established. However, few studies have assessed the prospective effects of traumatic events on changes in mental health symptoms. We analyzed data collected from adult residents of Detroit, Michigan between 2008 and 2010 to assess relations between exposure to traumatic events, including different types and number of events, and changes in depression severity during a one-year follow-up period. Participants in the first two waves of the Detroit Neighborhood Health Study (n = 1,054) reported traumatic event experiences in their lifetime and between study waves, and depressive symptoms were assessed for the month prior to each interview with the Patient Health Questionnaire-9 (PHQ-9; range 0-27 [most severe]). Using negative binomial regression adjusting for past month Wave 1 PHQ-9 score and other potential confounders, the mean PHQ-9 score at Wave 2 among those exposed to at least one traumatic event during follow-up (54.3% of the sample) was 1.75 times higher than the mean PHQ-9 score among those not exposed to any traumatic events ("mean ratio"; 95% confidence interval [CI] 1.30-2.36). Compared to no traumatic event exposure, specific exposures positively associated with depression severity were assaultive violence (mean ratio = 2.54, 95% CI 1.44-4.77), injuries and other directly experienced shocking events (mean ratio = 2.52, 95% CI 1.70-3.73), and a greater number of traumatic events (mean ratio for 3 or more events = 2.72, 95% CI 1.73-4.30). These results suggest that violence, injuries, and other directly experienced traumatic events play a considerable role in shaping depression severity and may be useful targets for interventions that could alleviate the substantial burden of depression in urban populations.

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DO TRAUMATIC EVENTS MEDIATE OR MODIFY THE RELATION BETWEEN NEIGHBORHOOD CONDITIONS AND DEPRESSION SEVERITY? *Melissa Tracy, Kara Zivin, Hal Morgenstern, Sandro Galea (Columbia University, New York NY 10032)

Persons living in adverse environments are more likely to report depressive symptoms. Traumatic event exposure may be a key mechanism through which neighborhood conditions influence depression. We used data from the first two waves of the Detroit Neighborhood Health Study to investigate the separate and joint effects of neighborhood characteristics and traumatic event exposure on depression severity (using the Patient Health Questionnaire-9 [PHQ-9]). Participants who had lived in their neighborhoods for at least one year at baseline (n = 1,037) were geocoded to the 54 Detroit Master Planning neighborhoods. We used multilevel logistic and negative binomial regression to estimate the effects of neighborhood conditions, traumatic events, and their interaction (heterogeneity of the mean PHQ-9 score ratio) on the Wave 2 PHQ-9 score, adjusting for Wave 1 PHQ-9 score and other potential confounders. Neighborhood disadvantage and low social cohesion were positively associated with depression severity; these relations were not mediated by traumatic events, which were only minimally associated with neighborhood characteristics. However, neighborhood conditions modified the estimated effects of traumatic events on depression severity. For example, in highly disadvantaged neighborhoods, the mean PHQ-9 score at Wave 2 was 3.8 times higher for those exposed to violence than for those not exposed to any traumatic event (95% Confidence Interval [CI] 1.6-9.2), but it was only 1.8 times higher in less disadvantaged areas [95% CI 1.1-5.3]) ($p < 0.001$ for interaction). These findings suggest that traumatic events are not an important mediator of the neighborhood-depression relation, but interventions to reduce depression after exposure to violence may best be targeted to those living in adverse environments.

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CHILDHOOD ADVERSITY, ADULT STRESSFUL LIFE EVENTS AND DEPRESSION: GUANGZHOU BIOBANK COHORT STUDY. *Michael Y Ni, ChaoQiang Jiang, Kar Keung Cheng, WeiSen Zhang, Tai Hing Lam, Gabriel M Leung, C Mary Schooling (School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR China)

The stress sensitization theory, where childhood adversity (CA) increases the vulnerability to depression following adult stressful life events (SLE), has been demonstrated in western settings. However, the association of CA with depression, and the applicability of stress sensitization in other populations are unclear. Multivariable logistic regression was used in cross-sectional analysis of older (≥50 years) men (n = 2,491) and women (n = 7,242) from phase 3 of the Guangzhou Biobank Cohort Study (2006-8) to assess the association of CA (4-item score) (n = 6,126 for none, 2,906 for 1 CA and 701 for ≥2CAs), and SLE (n = 9,289 for none, 444 for ≥1 SLE) with depression assessed from the Geriatric Depression Scale (GDS) (score ≥ 9). All associations were adjusted for age, sex, education and childhood socioeconomic position. Depression was present in 2.6% of the sample. Childhood adversity was associated with depression with a dose-response pattern from odds ratio (OR) 1.5 (95% confidence interval (CI) 1.2-2.0) for one CA to OR 3.6 (95% CI 2.5-5.0) for ≥2 CAs, compared with no CAs. These associations were similar after additionally adjusting for adult socio-economic position (longest held occupation and household income). SLE were associated with depression with OR 2.5 (95% CI 1.7-3.8) for ≥1 SLE compared with no SLE, adjusting additionally for occupation and income. Positive effect modification of SLE across strata of CA on GDS score was found on an additive scale ($p < 0.001$). CA and SLE were positively associated with depression in a non-western population in Southern China, possibly acting synergistically via stress sensitization. As modifiable risk factors for depression, CA and SLE are potential targets for the prevention of mood disorders.

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TEMPORAL ASSOCIATIONS BETWEEN RHEUMATOID ARTHRITIS DISEASE ACTIVITY AND THE ONSET OF PATIENT-REPORTED DEPRESSION. *Alan Rathbun, Leslie Harrold, George Reed (University of Massachusetts Medical School, Worcester MA 01655)

Background: Depression is a common comorbidity of rheumatoid arthritis (RA). Research into the temporal relationships regarding its onset has mainly focused on functional status. The study aim was to examine temporal associations of the diverse measures of RA disease activity (DA) with incident self-reported depression. Methods: The Consortium of Rheumatology Researchers of North America (CORRONA) registry is an observational cohort with longitudinal data on >34,000 RA patients. Cox regression was used to evaluate the associations of lagged time-varying DA with the onset of depression, defined as the first incident and persistent (two consecutive) reports of depression, in patients with no history of depression. DA metrics were the tender and swollen joint counts (TJC and SJC, respectively), patient (PT) and physician (MD) global visual analogue scale (VAS) assessments, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), converted health assessment questionnaire (cHAQ), PT-pain VAS, and a composite score, the clinical disease activity index (CDAI). Hazard ratios (HR) comparing 5th quintiles to 1st quintiles adjusting for demographic, behavioral, and clinical factors were estimated with 95% confidence intervals (CI). Results: All metrics of DA, except serum biomarkers (CRP and ESR), were associated with depression onset: CDAI HR = 2.4 [2.1-2.7]; PT-global VAS HR = 2.4 [2.2-2.8]; MD-global VAS HR = 1.8 [1.6-2.0]; TJC HR = 1.6 [1.5-1.8]; SJC HR = 1.4 [1.4-1.6]; PT-pain VAS HR = 2.3 [2.0-2.6]; cHAQ HR = 2.5 [2.2-2.8]. Effect sizes increased for persistent depression, by as much as 91%: PT-pain HR = 4.1 [3.1-5.4]. Conclusions: The data suggest depression onset in RA patients is related to measures reported by the patient: pain, functional status, and global DA; and measures derived solely from providers, rather than serum biomarkers. However, the magnitude of the associations was greater for PT measures, when compared to the MD assessments.

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MOOD DISORDERS, ANXIETY AND MIGRAINE HEADACHES: RESULTS FROM THE BRAZILIAN LONGITUDINAL STUDY OF ADULT HEALTH (ELSA-BRASIL). *Alessandra Goulart, Itamar Santos, Andre Brunoni, Maria Angelica Nunes, Valeria Passos, Paulo Lotufo (University of Sao Paulo, Sao Paulo Brazil)

Introduction: Previous studies suggest that mood disorders and anxiety are more prevalent among individuals with migraine compared to the general population. We aimed to verify if there is an association between mood/anxiety disorders and migraine diagnosis and frequency in a large multicentric cohort study, the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). Methods: Mental diagnoses were assessed using Clinical Interview Schedule–Revised (CIS-R). Migraine diagnosis was based on International Headache Society criteria for migraine and probable migraine. Migraine frequency was categorized as <1 /week (occasional migraine) or ≥1/week (frequent migraine). Chi-square/ANOVA tests were performed whenever applicable. Logistic models were performed to identify whether mood disorders were independently associated to migraine. Results: From a total of 15,105 cohort subjects, we evaluated 12,106 participants with complete information about headache and psychiatric disorders. Frequency of migraine (including probable migraine) was 63.3%. Of these, 52.2% had occasional migraine. Any mental disorder was diagnosed in 28.9%; the most often condition was generalized anxiety disorder (14.2%). Major depressive disorder (MDD) was present in 4.8% of participants. Migraneurs were younger than no migraneurs (55 vs. 50y-old, respectively). Two or more mood/anxiety diagnoses were present in 14%, 29.5% and 52.7% of individuals without headache, occasional migraine and frequent migraine, respectively ($p < 0.001$). In comparison to individuals without headache, the highest adjusted odds ratio (OR) was for the association between MDD and frequent migraine [OR 5.01; 95% CI 3.85-6.62], followed by the association between generalized anxiety disorder and frequent migraine [OR 4.33; 95% CI 3.64-5.15].Conclusions: Among migraneurs, an increase in the frequency of episodes had progressive stronger association with mood/anxiety disorders.

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PSYCHOSOCIAL OUTCOMES IN OEF/OIF VETERANS WITH PTSD: INITIAL FINDINGS FROM THE VALOR REGISTRY. *Shona C. Fang, Raymond C Rosen, Darren W Holowka, Brian P Marx, Jennifer J Vasterling, Heather Litman, Julia Akeroyd, Terence M Keane (New England Research Institutes, Inc., Watertown MA 02472)

Posttraumatic stress disorder (PTSD) is a common and disabling psychiatric disorder that affects a large number of active duty military personnel and veterans. Understanding psychosocial correlates and outcomes of PTSD in veterans is an important priority for allocating resources and targeting treatment for these servicemen and women. Using observational data from Project VALOR (Veterans After-Discharge Longitudinal Registry), a large national registry of veterans with and without PTSD, we examine psychosocial outcomes in association with PTSD, including the prevalence and severity of sleep disorders, alcohol abuse, anger reactions, depression or anxiety, functioning, and suicidality. VALOR is designed to assess the course of PTSD and related outcomes in combat-exposed male and female VA healthcare-seeking veterans who served in Operation Enduring Freedom (OEF) in Afghanistan or Operation Iraqi Freedom (OIF). 1,213 veterans with PTSD and 436 veterans without PTSD were enrolled (50% female). We describe outcomes by PTSD diagnosis as determined by electronic medical record. Compared to those without PTSD, veterans with PTSD were more likely to have reported anxiety (39% vs. 19%, $p < 0.001$) or depression (49% vs. 21%, $p < 0.001$). Further, veterans with PTSD had a significantly higher suicide risk compared to those without PTSD (14% vs. 6%, $p < 0.001$). Additionally, veterans with PTSD had evidence of poorer psychosocial functioning, increased sleep problems and marked interpersonal difficulties and anger control. In preliminary analyses of gender differences, males with PTSD were more likely than females to abuse alcohol and experience greater anger and hostility. Results provide strong evidence that veterans with PTSD are at higher risk of psychosocial comorbidities and related sequelae, including suicidality, when compared to veterans without PTSD, and highlight the importance of providing adequate treatment and support services for veterans with PTSD.

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THE ASSOCIATION BETWEEN LIFETIME POTENTIALLY TRAUMATIC EVENTS AND FORMAL AND INFORMAL CARE IN A POPULATION BASED SAMPLE OF ADULTS FROM LIBERIA. *Magdalena M Paczkowski, Margaret E Kruk, Leslie L Davidson, Stephen S Morse, Qixuan Chen, Sandro Galea (Columbia University, New York NY 10032)

Potentially traumatic events (PTE) are associated with healthcare use but in countries with two care systems, formal and informal, the relation between PTEs and care use is unclear. Informal care, provided by traditional healers and drug peddlers, may be costly and, in some cases, ineffective. Understanding the intersection of PTEs, formal, and informal care could inform health system responsiveness. We used a population based sample of 1,268 adults from Nimba County, Liberia to assess the relation between lifetime PTE experience quartiles, measured using the sum of Harvard Trauma Questionnaire events, and past year formal and informal care visits, operationalized as count data. We found that 76.8 % (95% Confidence Interval (CI): 74.5, 79.1) of respondents used both formal and informal care. In a Poisson regression model adjusted for demographics, experience of 13-16 (Incidence Rate Ratio (IRR) = 1.46, 95 % CI: 1.14, 1.87), 17-20 (IRR = 1.54, 95% CI: 1.18, 2.0), and more than 20 (IRR = 1.86, 95% CI: 1.4, 2.47) PTEs was associated with informal care compared to the referent of 0-12 PTEs. Experience of 17-20 (IRR = 1.4, 95 % CI: 1.2, 1.7) PTEs and more than 20 (IRR = 1.4, 95 % CI: 1.1, 1.8) increased formal care use compared to the referent. Among formal care users, the relation between all PTE quartiles and informal care was significant compared to the referent. Among those who used no informal care, experience of more than 20 PTEs (IRR = 2.57, 95% CI: 1.49, 4.43) was related to formal care. Overall, respondents complemented formal care with informal, highlighting use of care unlikely to decrease disease burden. Use of informal care by those with PTEs may reflect a lack of mental health services in formal care. Future work should explore determinants of formal care use by those with PTEs to elucidate why some complement formal care with informal, why others rely solely on formal care to meet their needs, and how formal care can be strengthened.

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CHRONIC MEDICAL CONDITIONS AND SERIOUS PSYCHOLOGICAL DISTRESS DURING PREGNANCY IN THE UNITED STATES. *Ahmed M Kassem, Nancy L Day (University of Pittsburgh, Pittsburgh PA 15261)

Psychopathology during pregnancy is a significant public health problem. Literature reported several risk factors for psychopathologic symptoms during pregnancy; however, few studies have explored how chronic medical conditions influence the risk of perinatal psychopathology. In these analyses, we were interested in the relation between three common chronic medical conditions (CMCs; Asthma, Diabetes and Hypertension) and past month serious psychological distress (SPD) during pregnancy in the United States. We pooled data of 3392 currently pregnant women from the 2008-2011 National Survey on Drug Use and Health (NSDUH), a cross-sectional nationally-representative annual survey. Covariates of interest included lifetime and past year CMCs, current trimester, age, race, marital status, education, employment, household income, insurance coverage, population density, past month substance use (cigarettes, alcohol, illicit drugs). After assessing bivariate associations between exposures and our outcome, we fit multivariable logistic regression models of past month SPD by lifetime and by past year CMCs, adjusted for potential confounders. We found that SPD was associated with both lifetime Diabetes (OR = 3.11, 95% CI 1.59-6.07) and lifetime Hypertension (OR = 1.90, 95% CI 1.17-3.07). SPD was not associated with either Asthma exposure variables but a statistically significant interaction was present between Asthma and cigarettes smoking. Our findings suggest that Diabetes and Hypertension and associated risk factors may function to increase risk of SPD during pregnancy. Chronic medical conditions are likely to influence the psychopathologic symptoms during pregnancy and future studies should explore possible mechanistic pathways.

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IMPROVING QUALITY OF LIFE AMONG HIV-INFECTED ADULTS: THE IMPORTANCE OF ADDRESSING DEPRESSION. *Angela Bengtson, Brian Pence, Julie O'Donnell (University of North Carolina, Chapel Hill, Chapel Hill NC 27599)

Depression affects 20-30% of people living with HIV (PLWH) and is associated with low quality of life (QOL). Addressing depression among PLWH may improve measures of QOL, including suicidality, HIV symptoms and interest in sexual activity. We analyzed data from 129 HIV+ adults with depression enrolled in a randomized controlled trial to evaluate the effectiveness of improved depression care on antiretroviral drug adherence. The exposure, change in depression score between baseline and 6 months, was measured using the Hamilton Depression Rating Scale (HAM-D). Change in depression was modeled continuously and using indicator variables for improvement or decline, compared to little or no change (referent). We used log-binomial and Poisson models with a robust variance estimator to estimate risk ratios (RR) for the relationships between change in depression and (1) improved suicidality (2)fewer number of HIV symptoms and (3)increased interest in sexual activity at 6 months. At 6 months, 42% (n = 54) of participants reported fewer HIV symptoms, 19% (n = 25) improved suicidality and 21% (n = 27) increased interest in sex. Each 5-unit change in depression score was associated with improved suicidality (RR 1.78; 95% CI 1.37, 2.31), adjusted for baseline partner status and psychiatric comorbidities. Improvement in depression was associated with fewer HIV symptoms (RR 1.34; 95% CI 0.90, 2.00), while worsening of depression was associated with more or stable HIV symptoms (RR 0.60; 95% CI 0.24, 1.47), adjusted for baseline CD4 count. Improvement in depression was not associated with an increased interest in sexual activity (RR 0.87; 95% CI 0.43, 1.74), but worsening depression was inversely associated with increased interest in sexual activity (RR 0.49; 95% CI 0.13, 1.92). Despite imprecision due to small sample size, our results suggest that treating depression in PLWH may improve a range of sexual, mental and HIV QOL measures.

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ASSOCIATION BETWEEN DEVELOPMENTAL TIMING OF EXPOSURE TO CHILD MALTREATMENT AND SYMPTOMS OF DEPRESSION AND SUICIDALITY: EVIDENCE OF A SENSITIVE PERIOD? *Erin Dunn, Katie McLaughlin, Natalie Slopen, Jonathan Rosand, Jordan Smoller (Massachusetts General Hospital, Boston MA 02215)

Background: Exposure to child maltreatment is a potent risk factor for depression and suicidality, two of the most serious public health problems in youth. While the timing of first exposure to maltreatment, or its age at onset, is considered an important dimension of the maltreatment experience that may be related to subsequent psychopathology risk, no consensus exists on whether earlier or later exposures are more deleterious. This study examined timing differences in the associations of exposure to physical and sexual abuse with depression and suicidality. Methods: Data were drawn from Waves 3 and 4 of the National Longitudinal Study on Adolescent Health. Age at first onset of physical and sexual abuse was classified as: early childhood (0-5), childhood (6-10), or adolescence (11-17). Depressive symptoms were measured using a 9-item version of the Center for Epidemiological Studies of Depression Scale. Suicidal ideation was measured with an item taken from the Youth Risk Behavior Surveillance system. Results: Respondents exposed to physical abuse at any age had a higher odds of depression and suicidal ideation than non-maltreated respondents. Among maltreated youth, exposure during pre-school (ages 3-5) was most strongly associated with depression. Participants first exposed to physical abuse during preschool had a 77% increase in the odds of depression and those first exposed to sexual abuse during early childhood had a 146% increase in the odds of suicidality compared to respondents maltreated as adolescents. Conclusion: We find that early maltreatment is more strongly associated with risk for depression and suicidality than maltreatment occurring at later developmental periods. Findings underscore the need for measures of adversity that include information on developmental timing of exposure. Such information can help identify sensitive periods, and elucidate pathways linking childhood adversity to psychopathology.

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PTSD, DEPRESSION, AND SUICIDALITY IN A SAMPLE OF US SOLDIERS. *Richard Herrell, Paul Bliese, Charles Hoge (Walter Reed Army Institute of Research, Silver Spring MD 20910)

Suicide is the principal cause of death attributable to psychopathology, and symptoms of suicidality are common in psychiatric disorders. Nevertheless, evidence of clear correlates of particular symptoms with suidality remains elusive. We administered a survey to 1664 male US Soldiers in garrison between deployments to Afghanistan that included measures of PTSD (the PCL), and depression (the PHQ-9) during the current month. Four questions addressed suicidality: "In the past year did you [1] often think a lot about death; [2] seriously think about committing suicide; [3] make a plan for committing suicide?" The 4th item asked if the respondent had attempted suicide over the lifetime. In order to examine which symptom profiles of PTSD and depression might better predict suicidality, we parameterized PTSD and depression by their Diagnostic and Statistical Manual-IV criteria. For PTSD, we used reexperiencing of the traumatic events, numbing of responsiveness, and increased arousal as separate variables; for depression, 8 of the criteria (excluding suicidal ideation, plans, or attempts) as separate variables. In logistic models, among the PTSD criteria only numbing and among the depression criteria, only feelings of guilt independently predicted seriously thinking about suicide, making a plan, or either of these two. For either of the two criteria, the adjusted odds ratio (OR) for numbing was 5.9 (95% confidence interval [CI] = 2.2-16.1; for guilt the OR was 5.2, CI = 2.3-11.7. Lifetime attempt confounded but did not modify these associations. Demographic variables did not affect the associations. The symptoms of PTSD but not depression modestly increased the odds of general ruminating about death. These results suggest that in a population of Soldiers with recent experience of war, subsyndromal presentation of PTSD and depression with these two criteria (numbing and guilt) may be associated with greater odds of thoughts and plans of suicide.

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TOTAL BLOOD MERCURY LEVELS AND DEPRESSION IN THE UNITED STATES: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2005-2008. *Tsz Hin Ng, Jana Mossey, Brian Lee (Drexel University School of Public Health, Philadelphia PA 19102)

Background: Mercury is a ubiquitous neurotoxicant that has been linked with psychiatric symptoms under high levels of exposure. However, it is unclear whether an association between mercury and depression is present at the typically low levels of mercury exposure found in the US general population. Methods: Cross-sectional associations of total blood mercury and depression were assessed in 6,911 adults over age 19 in the National Health and Nutrition Examination Survey (NHANES), 2005-2008. The Patient Health Questionnaire-9 was used to screen for depression (high likelihood of a depressive spectrum disorder diagnosis; score 5-27). Survey-weighted logistic regression models were used to examine the relationship between total blood mercury and depression. Results: Unadjusted analysis of the full sample suggested that higher total blood mercury was associated with lower odds of depression ($p < 0.05$; Odds Ratio = 0.49, 95% Confidence Interval: 0.36-0.65, comparing the highest to the lowest total blood mercury quintiles). This association largely disappeared after adjustment for the sociodemographic variables of income-poverty ratio, education, and marital status. However, in age-stratified analyses, this inverse relationship remained in older adults (age 40 or above) even after adjustment for sociodemographic variables. Simulation analyses adjusting for the expected confounding effects by fish intake suggested that the inverse relationship among older adults may be plausibly attributed to residual confounding. Conclusions: In the US household population, adults with a higher total blood mercury level did not show an increased risk of depression. The lower risk of depression observed among older individuals with a higher total blood mercury may be due to residual confounding.

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RACIAL/ETHNIC DIFFERENCES IN THE RELATION BETWEEN SEVERE CHILDHOOD ADVERSE EVENTS AND ADOLESCENT MENTAL HEALTH DISORDERS. Jennifer Ahern, *Deborah Karasek, Tim A Bruckner (School of Public Health, University of California, Berkeley CA 94720)

Background: Despite disparities observed in both severe adversities and physical morbidity faced by African Americans and Hispanics relative to whites, these racial/ethnic groups exhibit similar prevalence of psychopathology to whites. We examine whether there are racial/ethnic differences in the relation between severe adverse events in childhood and mental health disorders in adolescence. Methods: Using data from the National Comorbidity Survey–Adolescent Supplement (NCS-A), a nationally representative survey of 10,123 adolescents aged 13 to 18 years, we assessed DSM-IV classifications of mood, anxiety, behavior, and substance use disorders. Our exposure of interest, an index of severe childhood adverse events, included: parent death including suicide, parent in prison, physical abuse by parent, rape, and sexual molestation. Results: Whereas severe adversities were more common among African Americans and Hispanics than among whites, DSM-IV disorder prevalence was similar across race/ethnicity. In the full population, the adverse events index (range 0-3) was positively associated with psychopathology in logistic regression models that adjusted for parent's income and education, age, gender, and parental mental health. Adverse events were positively associated with mood disorders among whites [odds ratio (OR) = 1.59 95%CI (1.20, 2.11)] but not among African Americans or Hispanics. Adverse events were also associated with substance use disorders among whites [OR = 2.05 95% CI (1.69, 2.49)] and African Americans [OR = 2.14 95%CI (1.30, 3.53)] but not Hispanics. For all three groups, there were positive associations of adverse events with anxiety disorders and behavioral disorders, although the strength of the relation differed by race/ethnicity. Conclusion: The strong but differential mental health responses to childhood adverse events suggest buffering factors that may be differentially distributed by race/ethnicity and should be examined in future research.

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POSTTRAUMATIC STRESS DISORDER SYMPTOMS AND FOOD ADDICTION IN WOMEN, BY TIMING AND TYPE OF TRAUMA EXPOSURE. *Susan Mason, Karestan Koenen, Andrea Roberts, Alan Flint, Jessica Agnew-Blais, Janet Rich-Edwards (Harvard Medical School, Boston MA 02120)

Background: Post-traumatic stress disorder (PTSD) is a potentially important risk factor for obesity and obesity-related diseases, but the mechanisms linking PTSD to weight gain remain unclear. Emerging animal and clinical evidence suggests that chronic stress may provoke consumption of high-calorie foods, triggering dopaminergic reward systems that counteract feelings of distress. Over the long term, this eating pattern is associated with addiction-like behaviors and brain adaptations in rats, thus some stress-related overeating may constitute 'food addiction.' We examined the association of lifetime PTSD symptoms and age at PTSD onset with a measure of current food addiction in 2009 in the Nurses' Health Study II (NHSII). Methods: The NHSII ascertained timing of trauma exposure and PTSD symptoms in 2008 and current food addiction in 2009. Food addiction was defined as >3 clinically significant symptoms on a modified version of the Yale Food Addiction Scale. Confounder-adjusted prevalence ratios (PRs) and 95% confidence intervals (CIs) were estimated using modified Poisson regression. Results: Of 49,408 women in the study sample, approximately 80% reported some type of trauma exposure, with 66% of the trauma-exposed reporting at least 1 lifetime PTSD symptom. Eight percent of the cohort met the criteria for food addiction. There was a dose-response relationship between number of lifetime PTSD symptoms and food addiction. Women with the greatest number of PTSD symptoms (6-7 symptoms) had more than twice the prevalence of food addiction as women with no PTSD symptoms (PR = 2.66; 95% CI: 2.37, 2.98). PTSD symptoms were more strongly related to food addiction when symptoms began at an earlier age. In addition, PTSD symptoms in response to childhood physical abuse were more strongly related to food addiction than PTSD symptoms in response to other traumas. Conclusion: PTSD symptoms are associated with an increase in food addiction prevalence in women.

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CHILDHOOD ADVERSITY IS ASSOCIATED WITH PSYCHIATRIC DISORDERS, ANXIETY SYMPTOMS AND SUBSTANCE USE.

*Nancy CP Low, Nastasija Lezaic, Erika Dugas, Igor Karp, Jennifer O'Loughlin (McGill University, Montreal QC Canada)

Childhood adversity (CA) is associated with mood disorders in clinical settings. Less established is the relationship of more common forms of adversity (e.g. family death, illness, separation from parents by death or foster home) and a range of mental health and substance use outcomes. This examines the association between CA and (1) psychiatric disorders, anxiety symptoms, and substance use; (2) specific psychiatric disorders including mood disorders (bipolar, depression) anxiety disorders and alcohol or drug problems; (3) self-reported symptoms of depression, panic, generalized anxiety disorder (GAD), social phobia and agoraphobia; (4) use of specific substances. A school-based prospective cohort of 1293 students was followed 22 times over 13 years between the ages of 12-24 years. CA was collected from 642 parents. Diagnosed psychiatric disorders and symptoms and substances used were collected from 880 cohort participants who completed the 21st cycle of data collection. The association between number of childhood adversities and number of disorders, substances and symptoms was examined in logistic regression analyses. The CA experienced ranged from 2% for death of mother to 68% for other family death. In the presence of ≥3 adversities, there was a 3.5-fold increase in diagnosed mood disorders (depression, bipolar disorder) and a 3-fold increase in anxiety disorders and alcohol or drug problem. CA was also associated with a 2.5-fold increase in self-reported depression, panic, GAD and social phobia symptoms; 2-fold increase in social phobia symptoms, and lifetime use of specific drugs (marijuana, speed, ecstasy, cocaine) ranging from a 1.5 to 2-fold increase. CA is associated with mental health problems (depressed mood, anxiety) and substance use in adolescents and young adults. Strategies to detect childhood adversity and intervene to protect against possible mental health consequences should be developed.

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RECIPROCAL ASSOCIATIONS BETWEEN CONDUCT PROBLEMS AND DEPRESSION IN A COMMUNITY SAMPLE OF ADOLESCENT YOUTH.

*Isaac Rhew, Daniel Almirall, Ann Vander Stoep, Elizabeth McCauley (University of Washington, Department of Psychiatry and Behavioral Sciences, Seattle WA 98105)

Research on associations between conduct problems and depression among youth has generally shown support for conduct problems as a risk factor for later depression, but less support for the reverse pathway. Most studies, however, assessed psychopathology as the exposure at only one point in time rather than as a time-varying predictor. We examined the reciprocal associations between conduct problems and depression over repeated visits during adolescence using marginal structural models. Data were from a community-based prospective cohort study of 521 6th grade students assessed every 6 months for 3 years. When analyzed as exposures, psychopathology scores were dichotomized to indicate elevated symptoms. Stabilized inverse probability of exposure weights were calculated for each exposure according to prior history of time-varying and baseline covariates. Corresponding weights were applied to separate generalized estimating equation models with a negative binomial distribution that estimated the effect of elevated conduct problems on later depression and the effect of elevated depression symptoms on later conduct problems. Results from the weighted model indicated that when estimating the joint effects of conduct problems at 6- and 12-months prior, conduct problems at 12-, but not 6-, months earlier were associated with depression symptoms (Rate ratio (RR) = 1.31; 95% CI: 1.01-1.69). Examining the reverse pathway, statistically significant effects on conduct problems were observed for elevated depression symptoms 6 months prior (RR = 1.40; 95% CI: 1.08-1.81), but not 12 (RR = 1.18; 95% CI: .96-1.47). When using traditional non-weighted regression models adjusted for covariates, estimates were attenuated and no longer statistically significant for both pathways. These results suggest that conduct problems and depression may be sequentially related. Consideration of timing of interventions on one to prevent the other may be important.

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COPING STYLE AS A MODIFIER OF THE RELATIONSHIP BETWEEN SEVERE LIFE STRESSORS AND SUICIDAL IDEATION AMONG HIV-POSITIVE INDIVIDUALS WITH DEPRESSION.

*Julie O'Donnell, Brian Pence, Quinn Williams, Angela Bengtson, Riddhi Modi, Kristen Shirey, Bradley Gaynes (University of North Carolina-Chapel Hill Gillings School of Global Public Health, Chapel Hill NC 27514)

Depression and stressful life events are more common among HIV-infected individuals than the general population. Suicide is the most severe complication of depression; recognition of predictors of suicidal ideation (SI) is important for prevention. A randomized controlled trial testing the effect of evidence-based decision support for depression treatment on antiretroviral adherence (the SLAM DUNC study) includes monthly assessments of incident moderate and severe stressful life events. SI (Hamilton Rating Scale for Depression) and coping styles (Brief COPE Inventory) are assessed every 3 months. We examined the association between severe stressful events (SSEs) and SI for the first 3 months of study participation. Coping style was identified a priori as a potential modifier of interest. Among 69 individuals with complete data to date, 19 (28%) reported SI and 47 (68%) reported ≥1 SSE at 3 months. SI was reported by 26% and 29% of those with and without ≥1 SSE, respectively (prevalence ratio (PR) = 0.90, 95% CI = 0.42, 1.93). Among those with lower and higher adaptive coping scores, the PR (95% CI) was 1.55 (0.55, 4.32) and 0.24 (0.05, 1.16), respectively (homogeneity p-value = 0.05). After adjustment for baseline depression severity, psychiatric comorbidities, and marital status, using logistic regression due to model convergence issues, the odds ratio (95% CI) was 2.74 (0.50, 15.13) among those with lower coping scores compared to 0.05 (0.00, 0.91) among those with higher scores (homogeneity p-value = 0.02). The association between SSEs and SI appears to be modified by coping style. For those with less adaptive coping styles, experiencing severe stressors may increase SI risk; for those with more adaptive coping styles, severe stressors are associated with lower SI risk, perhaps due to activating coping mechanisms. Although our small sample size resulted in imprecise estimates, the apparent modification by coping style merits further study.

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POLYMORBIDITY: LOOKING BEYOND PTSD AND TBI IN RETURNING SERVICE MEMBERS AND VETERANS.

*Jennifer Fonda, Sara Lippa, Catherine Fortier, William Milberg, Regina McGlinchey (Translational Research Center for TBI and Stress Disorders (TRACTS), VA Boston Healthcare System, Boston MA 02130)

Background: With high rates of exposure to psychologically traumatic events and improvised explosive devices during Iraq and Afghanistan deployment, returning service members are at increased risk of polymorbid psychological disorders and traumatic brain injury (TBI). The present study aimed to determine how mild TBI (mTBI) and psychiatric comorbidities relate to overall functioning. Methods: *Participants*: TRACTS cohort of 190 Iraq and Afghanistan service members and veterans (average age of 33 (SD = 8.6) and 86% males). *TBI and Psychiatric Assessment*: Structured TBI interview, Clinician-Administered PTSD Scale, Structured Clinical Interview for DSM Disorders. *Outcome*: Overall and specific community level functioning, measured using the World Health Organization Disability Assessment Schedule II. Scores range from 0 to 100, with higher scores indicating worse functioning. *Covariates*: Age, sex, education, combat exposure, pain and sleep. Results: The highly prevalent, co-occurring current conditions include posttraumatic stress disorder (PTSD; 59%), mTBI (39%), depression (31%), anxiety (21%), and substance use (17%). 54% of participants presented with >2 comorbidities. The adjusted means and standard errors (SE) for general functioning, comparing those with the condition to those without: depression [41.8 (SE = 4.2) vs. 5.9 (SE = 2.1); p < 0.0001], PTSD [26.5 (SE = 2.6) vs. 3.8 (SE = 3.6); p < 0.0001]; anxiety [32.7 (4.5) vs. 13.0 (SE = 1.5); p = 0.001]; substance abuse [32.2 (SE = 5.4) vs. 13.8 (SE = 1.5); p = 0.006] and mTBI [20.0 (SE = 1.4) vs. 15.5 (SE = 1.1); p = 0.022]. These conditions showed similar results for specific areas of community level functioning. Conclusion: Returning veterans and service members presented with multiple comorbidities, all of which are important to consider in treatment, as they all relate to general and specific community level functioning.

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MARIJUANA ABUSE AND DEPENDENCE AND COGNITIVE DECLINE FROM CHILDHOOD TO MIDLIFE. *Jessica Agnew-Blais, Larry J Seidman, Stephen L Buka (Harvard School of Public Health, Boston MA 02115)

Introduction: Marijuana use has short-term effects on cognition, but whether these effects are long-lasting is under debate. A recent longitudinal study found marijuana use in adolescence was related to a decline in cognition into adulthood.1 However, it has been suggested that this finding could be due to confounding.2 Here we examine whether marijuana dependence/abuse is related to cognitive decline into midlife. Methods: This study includes 1,398 individuals from the New England Family Study who received IQ testing at age 7 and at adult follow-up (ave. = 39.5 years). IQ in adulthood was estimated using the vocabulary test of the Wechsler Adult Intelligence Scale; IQ in childhood was measured using the Wechsler Intelligence Scale for Children. Marijuana abuse/dependence was assessed through recall at time of adult interview. Results: 68 (4.9%) subjects met diagnostic criteria for lifetime marijuana dependence and 231 (16.5%) for marijuana abuse. Lifetime diagnoses of marijuana dependence/abuse were not associated with adult IQ after controlling for child IQ. Number of years of marijuana abuse was significantly related to adult IQ after controlling for childhood IQ, SES, and adult educational attainment (beta = -0.35, p = 0.009), although this was attenuated after controlling for years of alcohol abuse (beta = -0.21, p = 0.18). Conclusion: Lifetime diagnosis of marijuana abuse or dependence was not associated with a decline in IQ. However, there was a suggestion that longer duration of marijuana abuse was negatively associated with adult IQ, although this may be at least partially explained by comorbid alcohol abuse. 1. Meier MH, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci USA 2012;109(40):E2657-E2664. 2. Rogeberg O. Correlations between cannabis use and IQ change in the Dunedin cohort are consistent with confounding by socioeconomic status. Proc Natl Acad Sci USA 2013; Epub ahead of print.

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DECOMPOSING SOCIAL CAPITAL INEQUALITIES IN HEALTH. *Spencer Moore, Steven Stewart, Ana Teixeira (Queen's University, Kingston ON Canada)

Background: Research has shown network social capital associated with a range of health behaviours and conditions, including self-reported health (SRH) and physical inactivity. Little is known however about the sociological and psychological factors which contribute to inequalities in network capital and health. Knowledge about such factors can contribute to the design of interventions that can reduce network capital inequalities in health. Methods: Data come from the Montreal Neighbourhood Networks and Healthy Aging Study (n = 2707). A position generator was used to collect data on network social capital. Separate decomposition analyses of SRH, physical inactivity, and hypertension were conducted. The contributing role of sociodemographic, socioeconomic, socio-relational, and psychological factors were examined. The percentage contributions of sociological and psychological factors in explaining inequalities in health were calculated. Results: The percentage contribution of sociological and psychological factors varied according to the specific health or health behaviour decomposed. Across the three health outcomes, however, higher education emerged as contributing most to explaining network capital inequalities in health: 31% to SRH; 15% to physical inactivity; and 53% to hypertension. Social isolation explained 18.4% of network capital inequalities in hypertension. Conclusions: Network capital inequalities in health emerge from a range of sociological and psychological factors. Population health interventions that address social inequalities in education may also help to reduce network capital inequalities in health.

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SOCIAL AND GEOGRAPHICAL INEQUALITIES IN SUICIDE IN JAPAN FROM 1975 THROUGH 2005: A CENSUS-BASED LONGITUDINAL ANALYSIS. *Etsuji Suzuki, Saori Kashima, Ichiro Kawachi, S. V Subramanian (Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan)

Despite advances in our understanding of the countercyclical association between economic contraction and suicide, less is known about the levels of and changes in inequalities in suicide. We aim to examine social and geographical inequalities in suicide in Japan from 1975 through 2005. Based on quinquennial vital statistics and census data, we analyzed the entire population aged 25 to 64 years. The total number of suicides was 75,840 men and 30,487 women. For each sex, we estimated odds ratios (ORs) and 95% credible intervals (CIs) for suicide using multilevel logistic regression models with *cells* (cross-tabulated by age and occupation) at level 1, seven different years at level 2, and 47 prefectures at level 3. Prefecture-level variance was used as an estimate of geographical inequalities in suicide. Adjusting for age and time-trends, the lowest odds for suicide was observed among production process and related workers (the reference group) in both sexes. The highest OR for men was 2.52 (95% CI: 2.43, 2.61) among service workers, whereas the highest OR for women was 9.24 (95% CI: 7.03, 12.13) among security workers. The degree of occupational inequalities increased among men with a striking change in the pattern. Among women, we observed a steady decline in suicide risk across all occupations, except for administrative and managerial workers and transport and communication workers. After adjusting for individual age, occupation, and time-trends, prefecture-specific ORs ranged from 0.76 (Nara Prefecture) to 1.36 (Akita Prefecture) for men and from 0.79 (Kanagawa Prefecture) to 1.22 (Akita Prefecture) for women. Geographical inequalities have increased primarily among men since 1995. The present findings demonstrate a striking temporal change in the pattern of social inequalities in suicide among men. Further, geographical inequalities in suicide have considerably increased across 47 prefectures, primarily among men, since 1995.

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STRESSFUL SOCIAL RELATIONS AND MORTALITY. IS THE EFFECT MODIFIED BY SOCIO-ECONOMIC STATUS AND GENDER? *Rikke Lund, Ulla Christensen, Charlotte Juul Nilsson, Margit Kriegbaum, Naja Hulvej Rod (Institute of Public Health, University of Copenhagen, Copenhagen Denmark)

Few studies have addressed the relationship between stressful aspects of social relations and all cause mortality and they have primarily been focused on the closest confidant. We aim to address the association between conflicts with and worries/demands from partner, children, other family, friends and neighbors and all-cause mortality and to investigate the possible interacting effects with socio-economic status (SES) and gender. The 8,708 participants in Danish Longitudinal Study on Work, Unemployment and Health aged 36-52 years responded to a questionnaire in 2000 and were linked to the Danish Cause of Death Registry for all-cause mortality until 31st December 2011. Those who *always* (Hazard Ratio = 1.93; 95% CI: 1.02-3.65) or *often* (HR = 1.81; 1.23-2.67) experienced worries/demands from their partner had a higher mortality risk after adjustment for age, gender, SES, cohabitation status and prior hospitalization compared to those who did not. Frequent worries/demands from children were also associated with higher mortality risk (HR = 1.55; 1.08-2.20). The experience of conflicts with any type of social relations was associated with higher mortality e.g. conflicts with partner (HR = 2.19; 1.49-3.21), friends (HR = 2.63; 1.16-5.93) or even neighbors (HR = 3.07; 1.49-6.32). Further adjustment for depressive symptoms did not change the overall conclusions. There appeared to be an interaction between SES and strain from partner or friends. For example the joint exposure to both low SES and conflicts with partner was associated with a markedly higher mortality risk (HR = 4.52; 2.87-7.12) than expected from their individual effects. Interaction between gender and strain from partner, friends or neighbors was also suggested, with men exposed to high levels being in markedly increased risk of premature death. Stressful social interactions are associated with higher mortality risk across several social roles, and appear to interact with SES and gender.

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COMPOSITION AND CONTEXT IN THE ASSOCIATION BETWEEN AREA-LEVEL SOCIOECONOMIC STATUS AND CANCER INCIDENCE AND MORTALITY. *Theresa Hastert, Emily White, Shirley Beresford, Lianne Sheppard (Fred Hutchinson Cancer Research Center, Seattle WA 98109)

The purpose of this study is to estimate the association between area-level SES and total and site-specific cancer incidence and total cancer mortality and to assess whether any observed associations are explained by compositional factors including individual education and household income. Participants included 60,756 men and women ages 50-76 years who were recruited into the VITamins And Lifestyle (VITAL) Study cohort between 2000-2002. We identified the census block groups of participants and constructed an area-level SES index including data on income, education, housing and employment characteristics using data from the 2000 U.S. Census. Cox proportional hazards models were used to estimate the association between quintile of area-level SES and first cancer diagnoses (n = 6,099) and cancer deaths (n = 2,487) tracked through the Western Washington Surveillance, Epidemiology and End Results (SEER) database and the Washington State death file, respectively, through December 31, 2010. After controlling for age, sex, race/ethnicity, and marital status, living in areas in the lowest quintile of area-level SES index was associated with increased incidence of lung cancer (hazard ratio (HR): 2.21, 95% confidence interval (CI): 1.69-2.90) and colorectal cancer (CRC) among men (HR: 1.75, 95% CI: 1.14-2.70) and total cancer mortality (HR: 1.68, 95% CI: 1.47-1.93) compared with living in areas in the highest quintile of area-level SES. Further controlling for compositional factors including individual education and household income weakened but did not eliminate these associations (HR for lung cancer: 1.43, 95% CI: 1.07-1.91; HR for CRC among men: 1.53, 95% CI: 0.99-2.38; HR for total cancer mortality: 1.28, 95% CI: 1.11-1.48). Living in low-SES areas is associated with increased lung cancer incidence, increased CRC incidence among men, and higher total cancer mortality. These associations are largely, but not completely, explained by compositional factors.

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WORK CONDITIONS AND ORAL HEALTH: J-SHINE (JAPANESE STUDY OF STRATIFICATION, HEALTH, INCOME, AND NEIGHBORHOOD) STUDY. *Toru Tsuboya, Jun Aida, Ken Osaka (Tohoku University, Sendai Miyagi Japan)

Little is known regarding the association between work conditions and oral health in Japan. Using data form J-SHINE, which was conducted from Oct 2010 to Feb 2011 in four cities around Tokyo, we examined associations between work conditions and self-rated oral health (SROH) and tooth loss (TL) among 4,385 men and women aged 25 to 50 years. Work conditions were defined by both whether an employee is a specialist, whether an employee is white- or blue-collar, and whether a company has more than 1,000 employees, leading to nine categories; specialists, white-collar employees in large-scale companies, white-collar employees in medium and small companies, self-employed white workers, blue-collar employees in large-scale companies, blue-collar employees in medium and small companies (BM), self-employed blue workers, farmers, and others. SROH was assessed as follows: "*Overall, how would you rate the health of your teeth and gums - excellent, good, fair, not so good, or poor?*", and the responses were divided into two groups (excellent, good, and fair / not so good and poor). TL was binary. We used poisson regression to estimate the associations adjusted for age, sex, smoking, working hours, and job stress. The ratio of having poor SROH varied from 35.5% in worker in BM to 20.4% in specialists. Compared with specialists, workers in BM had significant higher prevalence rate ratio (PRR) of having poor SROH, 1.74 ($p < 0.01$) in univariate model and 1.57 ($p < 0.01$) in the multivariate model. Similarly, PRR of having TL was also significantly higher, 1.39 ($p < 0.01$) in univariate model, and 1.28 ($p < 0.01$) in multivariate model among BM workers. The high PRR of having poor SROH was attenuated to 1.46 ($p < 0.01$) when TL was added to the multivariate model. Our findings suggested that oral health inequalities exist across working conditions after adjusting for individual factors.

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WORK CONDITIONS AND HEALTH BEHAVIORS: J-SHINE (JAPANESE STUDY OF STRATIFICATION, HEALTH, INCOME, AND NEIGHBORHOOD) STUDY. *Toru Tsuboya, Jun Aida, Ken Osaka (Tohoku University, Sendai Miyagi Japan)

Little is known regarding the association between work conditions and health behaviors, although workers spend approximately half of their waking hours in their work places. Using data from J-SHINE (Japanese study of Stratification, Health, Income, and Neighborhood), which was conducted from Oct 2010 to Feb 2011 in four cities around the Tokyo metropolitan area, we examined associations between size and type of business and health behaviors, such as, smoking, alcohol consumption, physical inactivity and obesity, among 4,385 men and women aged 25 to 50 years. Work conditions were defined by both whether an employee is a specialist, whether an employee is white- or blue-collar, and whether a company has more than 1,000 employees, leading to nine categories; specialists, white-collar employees in large-scale companies, white-collar employees in medium and small companies, self-employed white workers, blue-collar employees in large-scale companies, blue-collar employees in medium and small companies (BM), self-employed blue-collar workers, farmers, and others. Health behaviors (smoking, alcohol drinking, physical inactivity) were assessed binary. We used poisson regression to estimate the associations adjusted for age, sex, smoking, working hours, and job stress. Working in BM was associated with increased risk of smoking [prevalence rate ratio (PRR) 1.88, $p < 0.01$], drinking [PRR 1.48, $p = 0.02$], and being obese [1.29, $p = 0.05$] in univariate model, comparing with specialists. Multivariate PRR were 1.44 ($p = 0.04$) for smoking, 1.25 ($p = 0.17$) for drinking, and 1.25 ($p = 0.09$) for being obese. Physical inactivity was not varied among the categories. Our findings suggested that some unhealthy behaviors were accumulated among workers in BM, and that high-risk strategy for such people to prevent cardiovascular diseases seems to be inequitable to reduce health inequalities.

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PERCEIVED NEIGHBORHOOD COHESION (NC) AND EDUCATION: INDIVIDUAL AND COMBINED EFFECTS ON DAILY SMOKING AND HEAVIER DRINKING IN HONG KONG CHINESE. *Brandford HY Chan, Hairong Nan, Paul H Lee, Michael Y Ni, Ian McDowell, TH Lam (School of Public Health, The University of Hong Kong, Hong Kong SAR China)

Objectives: The effect of perceived neighborhood cohesion (NC) on daily smoking/heavier drinking has not been previously examined among Chinese. This study examines the association between perceived NC, education, and daily smoking/heavier drinking, and assesses interaction between low NC and lower education on smoking/drinking. Methods: A randomly selected representative sample of 12,302 participants aged over 15 from the Hong Kong Jockey Club FAMILY Project was used. Perceived NC was defined as the perception of bonds among neighbors and measured using Sampson et al.'s five-item scale (1997). Heavier drinking was defined as alcohol consumption of more than 168 grams (for males) and 120 grams (for females) per week, or engagement in binge drinking in the past month. Synergy indices (SI) were used to examine the interaction effect between NC and education on smoking/drinking. Results: Low NC was associated with daily smoking (adjusted odds ratio (AOR) =1.51; 95% confidence interval (CI):1.18-1.92) and heavier drinking (AOR = 1.64; 95% CI = 1.13-2.38) among females only. Studying their combined effect, low NC was associated with smoking (AOR = 1.75; 95% CI: 1.35-2.26) and drinking (AOR = 1.66; 95% CI: 1.15-2.39) among females with secondary education only. The proportions of smoking/drinking were the largest among females with low NC and secondary education. This group also reported the largest odds to smoke (AOR = 5.49; 95% CI = 3.25-9.26) or drink (AOR = 1.77; 95% CI = 1.08-2.91). SI between low NC and secondary education were larger than 1, indicating that their combined effect is larger than the addition of their individual effects. Interaction accounted for 43% and 28% of the combined effect of low NC and secondary education on smoking and drinking, respectively. Conclusion: Females characterized by low perceived NC and lower education level are associated with higher odds of daily smoking or heavier drinking and may benefit from targeted prevention programs.

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THE ASSOCIATION BETWEEN CORTISOL CHARACTERISTICS AND NEIGHBORHOOD DISADVANTAGE IN A U.S. POPULATION-BASED SAMPLE OF ADOLESCENTS. *Kara Rudolph, Gary Wand, Elizabeth Stuart, Thomas Glass, Andrea Marques, Roman Duncko, Kathleen Merikangas (Johns Hopkins Bloomberg School of Public Health, Baltimore MD 21205)

Place may affect mental health through several pathways, of which biologic stress is one frequently invoked potential mediator. Recent studies have found associations between neighborhood conditions and cortisol (a stress biomarker), but overall findings have been mixed. This association is rarely studied in children and has been hampered by small sample size and racial/ethnic and geographic homogeneity. We estimated the association between neighborhood disadvantage and salivary cortisol levels in a large, geographically and racially/ethnically diverse subsample of adolescents from the National Comorbidity Survey Replication Adolescent Supplement (N = 2485). Salivary cortisol was collected before and after a modified Composite International Diagnostic Interview administered in the adolescent's home. We matched adolescents living in disadvantaged neighborhoods with those in non-disadvantaged neighborhoods to make the two groups similar on time and day of cortisol collection as well as demographic variables. Regression adjustment was performed on the matched data. Adolescents living in disadvantaged neighborhoods had marginally higher pre-interview cortisol levels (0.020 ng/mL, 95% Confidence Interval (CI) -0.005, 0.046) and steeper rates of decline in cortisol levels over the course of the interview (0.018 ng/mL/hr; 95% CI 0.002, 0.033) compared to similar adolescents in non-disadvantaged neighborhoods. There was no difference in post-interview cortisol levels. Marginally higher pre-interview levels and steeper slopes may reflect heightened reactivity to and recovery from novelty stress induced by the interview among adolescents living in disadvantaged neighborhoods.

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THE POSSIBLE EFFECT OF INCREASING NEIGHBORHOOD EDUCATION AND INCOME ON OVERWEIGHT/OBESITY, TYPE 2 DIABETES, AND SMOKING IN SAN FRANCISCO ADULTS. *Kelsey McDonald, J Michael Oakes (University of Minnesota, Division of Epidemiology and Community Health, Minneapolis MN 55454)

We employ propensity score matching (PSM) to minimize structural confounding and improve causal inference in an observational neighborhood effects study. We approximate a real-world scenario by creating causal contrasts where those in a higher socioeconomic status (SES) neighborhood quartile are matched with those in the next lower quartile. Typically studies split a sample into one exposed group and one unexposed group, or compare all lower groups to a single high group (or vice versa). Our approach yields more realistic policy estimates. We estimate the average effect of the treatment on the treated (ATT) moving from a lower to the next higher SES neighborhood quartile on overweight/obesity, type 2 diabetes, and smoking. Neighborhood SES is classified into quartiles of census-tract level median household income (NH income) and percent with bachelor's degree or higher (NH education). Individual-level covariate and outcome data from the 2005, 2007, and 2009 California Health Interview Survey (CHIS) for San Francisco adults (n = 2,515) was linked with census-tract level SES data from the American Community Survey (2006-2010). PSM results suggest a significant difference in ATT only when moving from the moderate-high to high NH education quartile for overweight/obesity (-0.10, 95% CI: -0.20 to -0.03) and smoking (-0.05, 95% CI: -0.12 to -0.03), using exchangeable exposure groups. We failed to find evidence of an effect for other comparisons using NH education. All comparisons using NH income were non-significant with estimates close to zero. The assumptions of observational neighborhood effects studies limit our ability to identify causal effects, but this study addresses some key challenges by using propensity score matching with policy-relevant causal contrasts.

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NEIGHBORHOOD SELF-SELECTION: THE ROLE OF PRE-MOVE HEALTH STATUS ON THE POST-MOVE SOCIOECONOMIC ENVIRONMENT. *Peter James, Jaime Hart, Francine Laden, SV Subramanian (Harvard School of Public Health, Cambridge MA 02138)

Background: A criticism of research on health impacts of area-based socioeconomic measures (ABSMs) is the concept of confounding by 'residential self-selection,' implying that individuals select neighborhoods by pre-existing health preferences. Aim: To estimate the magnitude of residential self-selection by analyzing pre-move health factors and the post-move socioeconomic environment. Methods: We used 1986-2008 data from the Nurses' Health Study, a nationwide prospective cohort. Our exposure was pre-move body mass index (BMI) (kg/m2) and metabolic equivalent hours of walking per week. Our outcome was post-move Census tract median income and household value based on the 2000 Census and assigned to each nurse based on her geocoded post-move residence. We conducted linear regression with each change of county as the unit of analysis. Results: There were 13,083 county moves over follow-up. Participants were all female, 94% white, and had a mean age of 64 years. The highest tertile of pre-move BMI was associated with a $6K (95% Confidence Interval $5K, $7K) lower Census tract post-move median income and a $26K ($22K, $31K) lower post-move median household value. The highest tertile of pre-move walking was associated with an $899 ($-75, $1,873) higher post-move median income and a $9K ($5K, $14K) higher post-move median household value. Based on a mean median household value of $170K (standard deviation (SD) $107K) and a mean median income of $63K (SD $23K), there was a moderate association between pre-move health behaviors and the post-move socioeconomic environment. Conclusions: We found some evidence of residential self-selection by ABSMs in this population.

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RACIAL DISCRIMINATION AND PRESCRIPTION DRUG PROBLEMS: EXAMINING ASSOCIATIONS AMONG URBAN ABORIGINAL ADULTS. *Cheryl Currie (Faculty of Health Sciences, University of Lethbridge, Lethbridge AB Canada)

Background: Little is known about factors associated with prescription drug problems within rapidly growing urban Aboriginal populations in North America. The objectives of this study were to examine whether racial discrimination was associated with 12-month prescription drug problems among urban-based Aboriginal adults in Canada. Methods: Data were collected via in-person surveys with a community-based sample of Aboriginal adults living in a mid-sized city in western Canada (N = 381) in 2010. The Drug Use Disorders Identification Test (DUDIT) was used to assess 12-month prescription drug problems. The Experiences of Discrimination Scale was used to measure 12-month racial discrimination. Results: More than 8 in 10 Aboriginal adults experienced discrimination due to Aboriginal race in the past year. More than half reported high levels (> 3 situations) in that time period. Almost 6% had scores suggestive of a prescription drug problem using a cut-off 2 standard deviations above the mean for this sample (DUDIT > 21). Racial discrimination was a significant risk factor for 12-month prescription drug problems. Prescription drug score increased one half point for each additional situation discrimination was experienced in the past year (B = 0.51, 95% CI = 0.11, 0.93) in a bootstrapped linear regression model adjusted for all relevant confounders. Discussion: This is one of the first studies to examine the extent to which Aboriginal peoples in Canada may experience racism. Findings suggest Aboriginal Canadians may experience very high levels of discrimination, and that racism may serve as a risk factor for prescription drug problems in this population. The findings of this study suggest improved policies to reduce racism directed at Aboriginal peoples in urban areas are needed.

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LITERACY AS MEDIATOR OF THE RELATIONSHIP BETWEEN EDUCATION AND MORTALITY. *Thu Nguyen, Eric Tchetgen, Ichiro Kawachi, Stephen Gilman, Stefan Walter, Maria Glymour (Harvard School of Public Health, Boston MA 02215)

Background: Many theorized mechanisms exist to explain the relationship between education and health. A hypothesized mechanism described by the quantity model is education confers skills and knowledge. Under the quantity model, greater years of schooling lead to the acquisition of more human capital. We focus on testing the quantity model and assess the extent to which the effect of education on mortality is mediated through one important skill acquired through schooling, literacy. Methods: The sample included 17,054 Health Retirement Study participants born in the U.S. between 1900 and 1947. In assessing literacy, respondents were asked to provide the definition of 5 words. Responses were recorded and coded according to the degree of accuracy. To estimate the total, natural direct, and natural indirect effects using the product method, we fit linear regression models and Aalen additive hazard models. All models were adjusted for age, sex, race, ethnicity, child health status, and region of birth. Results: A one standard deviation change in educational attainment (3 yrs) was associated with 6.8 (95% CI: -8.0, -5.6) fewer deaths per 1,000 person-years. Of this decrease, 1.2 (95% CI: -1.8, -0.7) fewer deaths per 1000 person-years were attributed to the literacy pathway. This represented 18% of the total effect, leaving the remaining 5.6 deaths/1000 person-year reduction (95% CI: -6.9, -4.2) as the natural direct effect. Future work will investigate exposure-mediator interactions and measurement error in the mediator. Conclusion: Education confers many benefits; as demonstrated by this study, one important benefit for health is literacy.

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THE RELATIONSHIP BETWEEN SOCIAL FRAGMENTATION AND SLEEP AMONG ADOLESCENTS LIVING IN BOSTON, MASSACHUSETTS. *Roman Pabayo, Beth Molnar, Renee Johnson, Ichiro Kawachi (Harvard School of Public Health, Boston MA 02115)

Only a minority of adolescents obtains adequate amounts of sleep needed for healthy growth and development. Although individual level correlates of sleep have been identified, knowledge regarding the influence of the environment on sleep and potential mechanisms of how the environment affects sleep among youth are warranted. The purpose of this study was to investigate relationships between area-level (SF) fragmentation and the likelihood of meeting the recommended amount of sleep and sleep duration among 1,878 urban adolescents living in 38 neighborhoods participating in the 2008 Boston Youth Survey (BYS), which is a biennial survey of high school students (grades 9-12). Also, we wanted to test whether alcohol consumption, smoking, and physical inactivity acted as mediators between SF and sleep. Participants were categorized into inadequate sleep (<8.5 hours) or adequate (≥8.5 hours). SF was composed of the following 2010 US Census indicators: proportion of residents who have lived in the same house less than 5 years, proportion of vacant house units, and proportion of owner occupied housing (reverse coded). Multilevel regression models were used to determine the association between neighborhood level social fragmentation and meeting the recommended hours of sleep (>8.5 hours) and sleep duration while controlling for individual-level sex, race, age, and immigrant status. Moderate (OR = 0.43, 95%CI = 0.19, 0.94) and high (OR = 0.49, 95%CI = 0.21,1.16) SF within the residential neighborhood was associated with a decreased likelihood of being obtaining adequate sleep. Those in a moderate (β = -23.3, 95% CI = -39.2, -7.5) and high (β = -19.0, 95% CI = -36.9,-1.1) SF schools obtained fewer minutes of sleep per night. These relationships were abated when mediators were included. SF may be an important determinant of sleep among youth living in urban settings. Neighborhood level interventions might be needed to help youth obtain adequate sleep.

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ORAL HEALTH DISPARITIES OF CHILDREN AMONG SOUTHEAST ASIAN IMMIGRANT WOMEN IN ARRANGED TRANSNATIONAL MARRIAGES IN TAIWAN. *Ying Chun Lin, Ping Ho Chen, Pi Li Lin, Chien Hung Lee, Hsiao Ling Huang (Kaohsiung Medical University, Kaohsiung Taiwan)

Taiwan has been faced with the migration of large numbers of women from Southeast Asian countries. Arranged intermarriage is one type of cross-border migration flow for women. This form of arranged transnational marriages has created a special phenomenon of marriage trades that is popular among the lower middle classes. The majority are from Vietnam and Indonesia. Southeast Asian wives is estimated approximately one-third of Taiwanese marriages. This study assessed the oral health care needs of children whose parents are Southeast Asian immigrant women in arranged transnational marriages. We used the baseline data of the Lay Health Advisor Approach to Promote Oral Health Program to explore disparities and associated factors in oral health among immigrant children. A cross-sectional community-based study was conducted to collect data from mothers and their children in Southern Taiwan in 2011. A total of 590 (440 natives, 150 immigrants) children aged 4-6 years and their mothers completed the questionnaire and oral examination. Multiple regression models analyzed the association between children oral health and related factors. The caries index was 6.05 in immigrant children and 3.88 in native children ($p < 0.001$). The caries prevalence of maxillary anterior teeth in the labial surfaces was higher among immigrants, ranging from 14.7% to 22%. The factor associated with children caries index was the maternal tooth-brushing frequency (adjusted odds ratio (aOR) = 8.95, 95% CI: 1.95-41.05). Mother did not direct child to brush teeth after eating sweets, their children were more likely to have decayed teeth (aOR = 3.54, 95% CI: 1.04-12.03). The findings suggest that culturally adequate oral health promotion intervention programs should be implemented for immigrants.

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EVALUATION OF A LAY HEALTH ADVISOR TRAINING FOR A COMMUNITY-BASED ORAL HEALTH PROGRAM IN IMMIGRANT MOTHERS. *Yuan Jung Hsu, Wu Der Peng, Chin Shun Chang, Chien Hung Lee, Hsiao Ling Huang (Kaohsiung Medical University, Kaohsiung Taiwan)

The 5-year Lay Health Advisors Approach to Promote Oral Health Program, aimed at promoting the oral health of new immigrants' children, was first implemented in Taiwan in 2011. Prior to this study, no oral health promotion programs for mixed-marriage preschool children and their mothers were conducted. The baseline data showed significant higher caries index in immigrant children aged 4 to 6 than in native children (6.05 vs. 3.88). The use of Lay Health Advisors (LHAs) to address health issues is well documented and considered an appropriate model of community health promotion. This study is to evaluate the effectiveness of LHA training program in immigrant mothers. There were 50 Vietnamese and Indonesia mothers recruited from the churches, Chinese language program and immigrant service centers in 2012. Four training classes were held. Each training cycle went for 15 consecutive weeks (one 2-hour training session per week) including 3 weeks practicum and each session was conducted by oral health professionals. The training manual includes caries-related knowledge, oral hygiene demonstration, teaching/communication skills and hands-on practice etc. Overall, 37 participants completed the program. The pre- and post-data were collected by the self-administered questionnaire. We used paired t test, McNemar exact test and marginal homogeneity test to analyze the data. The results showed significantly increased levels of oral health knowledge, self-efficacy and attitude toward oral hygiene. It also showed a higher frequency of brushing teeth a day, using dental floss a day, using fluoride toothpaste and children's dental visits in participants ($P < 0.05$). The results suggest that the LHA training program is effective in promoting oral health behaviors.

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AREA DISPARITY IN CHILDREN'S PERCEPTIONS OF ACCESS TO TOBACCO AND CIGARETTE-PURCHASING EXPERIENCES IN TAIWAN. *Heng Lee, Chien-Hung Lee, Wu-Der Peng, Hsiao-Ling Huang, Pi-Li Lin (Kaohsiung Medical University, Kaohsiung Taiwan)

Adolescents who perceive easy access to tobacco are more likely to acquire cigarettes and experience smoking. This study assesses area disparities in perceptions of access to tobacco, cigarette-purchasing experiences, and its related factors among elementary schoolchildren. Data on children's tobacco accessibility and related variables were obtained from the Control of School-aged Children Smoking Study Survey in 2009 in Taiwan. A stratified random sample of 65 primary schools was included; four classes were randomly selected from each grade of 3 to 6 (ages 8-13) from each school. A structured questionnaire was used to collect information. In total, 5,353 questionnaires were collected. Polytomous logistic regression analyzed the factors associated with tobacco accessibility and purchasing experiences. More than half of the children reported that tobacco retailers often or always sold cigarettes to them. Children from rural and mountainous areas were more likely to access to cigarettes [adjusted odds ratio (aOR) = 2.01 and aOR = 3.01, respectively] and have cigarette-purchasing experiences (aOR = 3.06 and aOR = 13.76, respectively). Tobacco retailer's selling tobacco to children (aOR = 1.84) was significantly associated with children's perception of access to tobacco. The other significant factors associated with cigarette-purchasing experiences were families smoking (aOR = 8.90), peers smoking (aOR = 2.22), frequent exposure to actors and actresses smoking on TV and in films (aOR = 2.15), and perceived access to tobacco (aOR = 1.51). It is suggested that the health department of government should strictly enforce the laws regarding retailers selling tobacco to adolescents so as to reduce underage access to tobacco, particularly in rural and mountainous areas.

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MISSING MEALS AMONG HIGH SCHOOL STUDENTS: PREVALENCE AND CORRELATES. *Zewditu Demissie, Danice Eaton, Richard Lowry, Allison Nihiser (Centers for Disease Control and Prevention, Atlanta GA 30341)

Previous research has demonstrated the benefits of eating breakfast regularly, but little is known about the prevalence and correlates of missing lunch or dinner. The purpose of this study is to determine the prevalence of missing breakfast, lunch, and dinner among high school students and the correlates of missing meals. Data were obtained from the 2010 National Youth Physical Activity and Nutrition Study, which included a survey administered to a nationally representative sample of students in grades 9–12 and measured height and weight. Univariate analyses were used to determine the prevalence and 95% confidence intervals (CIs) for missing ≥1 day of breakfast, lunch, and dinner during the past 7 days. Bivariate analyses were conducted to examine associations between demographics and missing meals. Logistic regression was used to estimate adjusted odds ratios and 95% CIs for associations between missing meals and lifestyle and dietary correlates. In 2010, 63.1% of high school students missed breakfast, 38.2% missed lunch, and 23.3% missed dinner ≥1 day during the past 7 days. Characteristics associated with higher prevalence of missing meals include female sex, non-Hispanic black race/ethnicity, obesity, perceived overweight, and video game/computer use. Associations with TV watching were mixed. Daily physical activity and sports participation were associated with lower odds of missing meals. Missing breakfast was associated with lower odds of fruit and vegetable intake and higher odds of sugar-sweetened beverage and fast food intake. No significant associations were found between missing lunch and dietary behaviors. Missing dinner was associated with decreased vegetable intake. While students should eat regular meals to maintain nutritional needs, prevention efforts for missing meals should focus on breakfast as this was the most frequently missed meal, and missing this meal was associated with the greatest number of less healthy dietary practices.

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EFFECTIVENESS OF SMOKING CESSATION METHODS AMONG CHINESE SMOKERS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS. *Hongying Shi, Xinjun Yang, Chenping Huang, Ziwei Liu, Xinyun Xu, Chong Lin (Department of Preventive Medicine, School of Environmental Science and Public Health, Wenzhou Medical College, Wenzhou China)

Background: To evaluate the effectiveness of smoking cessation methods in China, we conducted a systematic review and meta-analysis of published articles from randomized and quasi-randomized controlled trials. Methods: The PRISMA statement was used as a guide. Three electronic databases (PUBMED, CBM and CNKI) were searched from their start dates to December 2012. We included all trials comparing different smoking cessation methods among the Chinese mainland population. Primary outcomes were prevalence of smoking abstinence at different durations of follow-up. We used the risk ratio for summarizing individual trial outcomes and for estimates of pooled effect. Results: A total of 11,706 participants from 43 trials (38 in Chinese journals) were included; most of the articles were published within the last 3 years. Twenty-two trials were on patients (hospital-based); 8 trials were community-based; 4 trials were based at cessation clinics; the remaining 9 studies enrolled specialized participants. Ten studies evaluated different pharmacotherapies, the others focused on behavioral interventions. The main meta-analyses were performed on the patients groups. Almost all interventions offered treatment benefits over controls at most time points, and most cessation methods approximately doubled the chance for cessation while better outcomes were observed in patients as compared to general population. Conclusions: In the recent years, the number of publications on smoking cessation interventions in mainland China has dramatically increased. Although the results were based on trials conducted with heterogeneous populations, current evidence suggests that almost any smoking cessation intervention would yield a positive benefit on quit rate. Still, more research is required for determining cost-effective smoking cessation interventions in low to middle income countries like China. Funding: This work was funded by Philip Morris Products S.A.

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SNUS USE AND SMOKING BEHAVIORS AMONG ADOLESCENTS: IS SNUS ASSOCIATED WITH SMOKING INITIATION OR CESSATION? *Jim Jansen, Kelvin Choi, Jean Forster (University of Minnesota, Minneapolis MN 55454)

Introduction: Using survey data from the Minnesota Adolescent Community Cohort (MACC), we examine the characteristics associated with use of snus stratified by prior smoking status and investigate whether snus is associated with smoking initiation among non-smokers and cessation among smokers. Methods: 2,334 young adult participants (mean age = 22) who completed the 2008-2009 survey (baseline) and the 2010-2011 survey (follow-up) were included in this analysis (482 baseline smokers, 1154 baseline non-smokers). Independent variables include age, gender, race, education, smokeless tobacco marketing exposure, peer smoking, past year smokeless tobacco use and days smoked in the past 30. We examined first the predictors of snus use by baseline smoking status, then the association between snus use and smoking initiation or cessation at follow-up among baseline non-smokers and smokers, adjusting for all other independent variables. Results: Overall, men and those who had used smokeless tobacco in the past year were more likely to have tried snus at follow-up. Non-smokers exposed to smokeless tobacco marketing were more likely to have tried snus at follow-up (adjusted odds ratio = 2.80, 95% confidence interval 1.31-5.97), while no significant association was found among smokers ($p \geq 0.05$). Among non-smokers, those who used snus at follow-up were more likely to have initiated smoking compared to those who did not use snus (AOR = 4.37, 95% CI: 2.29-8.34). Among baseline smokers, no significant association was found between having tried or currently using snus and attempting to quit smoking ($p \geq 0.05$). Conclusions: Snus use appears to be associated with smoking initiation among non-smokers but not with smoking cessation among smokers, suggesting snus may provide additional opportunities for young adults to try using tobacco.

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ASSOCIATIONS OF ALLOSTATIC LOAD WITH SLEEP APNEA, SHORT SLEEP DURATION AND OTHER SLEEP PROBLEMS: FINDINGS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2005-2008. *Xiaoli Chen, Susan Redline, Alexandra E Shields, David R Williams, Michelle A Williams (Harvard School of Public Health, Boston MA 02115)

Background: Quality sleep is fundamental for health and wellness. We hypothesize that allostatic load (AL), a measure of cumulative physiologic dysregulation across biological systems, is associated with sleep problems. Methods: Data from the National Health and Nutrition Examination Survey 2005-2008, a nationally representative sample of 3,144 US adults aged ≥20 years, were used to examine cross-sectional associations of AL with sleep problems. Sleep problems included sleep apnea, insomnia, short sleep (sleep <6 hours), any sleep disorder diagnosed by a physician or other health professional, snoring, and snorting. AL was measured using 9 biomarkers. Multivariable logistic regression models were fit to adjust for potential confounders. Stratified analyses were conducted to examine whether observed associations varied by race/ethnicity and sex. Results: The frequency of high AL (AL score ≥ 3) was the highest among African Americans (25.3%), followed by Whites and Mexican Americans (both 17.1%), and other racial/ethnic group (13.8%). High AL was associated with sleep apnea (odds ratio (OR) = 2.02, 95% confidence interval (CI): 1.53-2.67), short sleep (OR = 1.41, 95% CI: 1.00-1.97), sleep disorder (OR = 2.45, 95% CI: 1.86-3.21), snoring (2.26, 95% CI: 1.75, 2.90), and snorting (OR = 2.20, 95% CI: 1.61-3.00). These associations persisted after adjustment for central obesity. There was a marginally significant association between high AL and insomnia (OR = 1.51, 95% CI: 0.96-2.37). Associations for sleep disorder were similar across racial-ethnic groups (Pinteraction = 0.168). There was some evidence of a stronger association of AL with snoring among women than men (Pinteraction = 0.048). Conclusions: Our findings suggest that high AL is associated with sleep problems such as sleep apnea and sleep apnea symptoms (snoring, snorting) in US adults. Prospective studies will allow for assessing possible bidirectional associations of allostatic load with sleep problems.

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SELF-REPORTED SLEEP DURATION AND KIDNEY FUNCTION: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2005-2010. *Wenyuan Li, Hannah Buettner, Elizabeth Mostofsky, Murray A Mittleman (Harvard School of Public Health, Boston MA 02115)

Background: Both long and short sleep duration have been associated with risk factors for chronic kidney disease (CKD) but the relationship between sleep duration and kidney function has not been well-examined. Methods: We used data from the National Health and Nutrition Examination Survey (NHANES) 2005-2010 (n = 7,644) to examine the association between short, normal, and long sleep duration (≤5, 6-8, ≥9 hours/night) and the prevalence of low estimated glomerular filtration rate (eGFR < 60 ml/min/1.73 m2), albuminuria (urine albumin:creatinine ratio (UACR) ≥ 30 mg/g) and CKD (low eGFR or albuminuria). We fit multivariable logistic regression models to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between short and long sleep duration with CKD, low eGFR and albuminuria. We adjusted for several demographic, socioeconomic, behavioral, clinical characteristics, biomarkers and hypnotic medication use. All analyses accounted for the complex survey sampling design. Results: CKD was more prevalent in participants reporting short (17.0%) and long (20.5%) sleep duration compared to those reporting normal sleep duration (12.3%). In adjusted models, the odds of CKD was higher for short (OR = 1.29, 95% CI 1.02-1.62) and long (OR = 1.37, 95% CI 1.00-1.88) sleep duration than 6 to 8 hours of sleep. Long sleep duration was associated with a higher odds of both albuminuria (OR = 1.19, 95% CI 0.85-1.68) and low eGFR (OR = 1.32, 95% CI 0.87-1.99) while short sleep duration was only associated with higher odds of albuminuria (OR = 1.44, 95% CI 1.10-1.89). Conclusion: In this study, sleep duration was associated with measures of kidney function even after adjusting for potential confounders. The association between short sleep duration and CKD was driven by albuminuria alone, while the association between long sleep duration and CKD involves both albuminuria and low eGFR. Longitudinal studies are required to better understand these relationships.

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EVALUATION OF A SHORT-TERM INTERVENTION ON CHANGING UNIVERSITY STUDENT'S ORAL SELF-CARE BEHAVIOR: A QUASI-EXPERIMENTAL DESIGN. *HL Lee, WD Peng, YY Yen, HL Huang (Kaohsiung Medical University, Kaohsiung City Taiwan (R.O.C.))

Approximately 99.17% of Taiwanese adults have gingivitis. Tooth plaque is one of the risk factors in periodontal diseases. One key factor in preventing periodontal disease is the regular dental floss to remove inter-dental plaque. Health care provider plays a critical role in helping to reduce and prevent disease. Nevertheless, the use of dental floss is below a desirable level (18.3%-37.4%) in health personnel. The aim is to examine the effectiveness of dental care intervention on the variables of Theory of Planned Behavior (TPB) and the adherence to regular flossing. The samples were recruited from a medical university in Taiwan. A quasi-experimental study was conducted in which 63 students in Public Health department were set up as the experimental group while 90 students in Medical Social Work department were the comparison group. Students in experimental group completed both action planning (a concrete plan of where, when, and how to floss) and coping planning (a way to overcome barriers to action). Floss use, variables of TPB and planning were collected by a self-administered questionnaire. Follow-up data including self-report floss use, residual floss, and planning were collected at the 2nd and 6th week after the intervention. Two sample t-test and Wilcoxon rank sum test analyzed the differences between experimental and comparison group. Results showed 49.18% increase in the use of dental floss within 1 month in experimental group after the intervention. We also found a significant difference between the two groups in dental floss behavior after the intervention had started for one month ($p < 0.01$). The level of behavioral belief, perceived power and the scores of planning in experimental group had a significantly increase from baseline to 1-month post-test. The findings provide evidence for the effects of short-term intervention on promoting oral self-care behavior in medical university students.

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ASSOCIATIONS BETWEEN THE ENVIRONMENT AND RECREATIONAL AND TRANSPORTATION PHYSICAL ACTIVITY IN THE PARIS REGION. *Noëlla Karusisi, Basile Chaix (Inserm U707 - University Paris 6, Paris France)

To investigate the physical activity behavior, we conducted three complementary studies that examined associations between environmental characteristics and informal recreational activity (jogging), formal recreational activities (requiring facilities), and transportation activity (commuting). We conducted cross-sectional analyses with the RECORD Cohort Study involving 7290 participants, aged 30-79 years, and residing in the Paris metropolitan area. Multiple environmental characteristics were measured and the spatial accessibility to sport facilities was assessed with two approaches that take into account the street network (distance and count of facilities). Active commuting was studied by geocoding the place of residence, the workplace and the supermarket. Markov chain Monte Carlo approaches were used to estimate multilevel models. After controlling for individual characteristics, high individual education was associated with a higher probability of jogging and with the practice of racket sports, swimming, and fitness over the previous 7 days. The presence/high quality of green and open spaces was associated both with a greater probability of jogging and with the practice of jogging within rather than outside one's neighborhood. Spatial accessibility to swimming pools was associated with swimming. High neighborhood income was associated with the practice of a racket sport and fitness. Moreover, a high social cohesion was associated with a higher probability of jogging. After determining the shortest path between the residence and the workplace and the supermarket with a Geographic Information System, we found that geographic characteristics of the neighborhood and of these paths were associated with the reported walking time to work and to shop. Our results suggest that physical activity is a multi-dimensional concept that integrates geographical, financial, and environmental aspects.

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BEHAVIORAL PREDICTORS OF SCREEN TIME AMONG HIGH SCHOOL STUDENTS IN MALDEN, MA. *Blessing Dube, Lisa Arsenault, Kelly Washburn, Emily Chiasson, Renee Cammarata Hamilton (Cambridge Health Alliance, Cambridge MA 02141)

Background: Excessive screen time has been associated with unhealthy behaviors in youth. A trend towards higher computer/video game use over television (TV) viewing has been observed, but little research has focused on comparison by type of screen. Objective: To examine health-related behavioral predictors (sleep duration, fruit and vegetable intake, physical activity) of screen time, by type among High School students in Malden, MA; a diverse community neighboring Boston, MA. Methods: In 2012, 1, 367 students completed a health survey based on the Youth Risk Behavior Survey. Logistic regression models of high screen time (>3 hours on an average school day) were constructed to test associations with behavioral predictors (low fruit/vegetable intake, low physical activity, and inadequate sleep) while adjusting for confounders (gender, race/ethnicity, weight status and grade). Results: 39% had high computer/video game use and 24% had high TV time. Results indicated students with low physical activity were more likely to have high computer/video game use (Odds Ratio (OR) = 1.40; 95% Confidence Interval (CI) 1.05 – 1.87), additionally Asian students were significantly more likely to have high computer/video game use. Whereas, students with inadequate sleep were less likely to have high TV time (OR = 0.6; 95% CI 0.41 – 0.87), Black/African American and Hispanic students were significantly more likely to have high TV time. Conclusion: Findings suggested associations with behavioral predictors differed by type of screen time and were not consistent with those reported historically in the literature, particularly for TV screen time. As media use changes among American youth, identification of these new patterns of behavior is crucial to understanding their impact on health and their potential as targets for policy change.

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EARLY LIFE AND SOCIAL FACTORS ASSOCIATED WITH GANG INVOLVEMENT AMONG STREET-INVOLVED YOUTH: A GENDER-BASED ANALYSIS. *Brandon Marshall, Kora DeBeck, Annick Simo, Thomas Kerr, Evan Wood (Brown University, Providence RI 02912)

Although the literature is limited, existing evidence suggests that gang involvement is associated with several adverse health outcomes among high-risk youth, including substance abuse, sexual risk behavior and unintended pregnancy. However, few studies have investigated the early life and social determinants that increase the risk for gang affiliation among this population. Elucidating these risk factors could have important implications for public health and safety efforts seeking to reduce gang violence and other related health problems. We examined the relationship between self-reported gang involvement and early childhood traumatic experiences, social factors, and other behaviors in a study of drug-using street-involved youth in Vancouver, Canada. Among 438 eligible participants, the mean age was 22, 77 (22.4%) were of Aboriginal ancestry and 125 (36.7%) were female. A total of 94 (21.5%) reported a lifetime history of gang involvement and 206 (48.1%) reported having friends involved in a gang. In gender-stratified log-binomial models, males involved in gangs were more likely to be of Aboriginal ancestry (prevalence ratio [PR] = 1.63, 95% confidence interval [CI]: 1.09 - 2.44), have grown up in an orphanage or foster home (PR = 2.03, 95% CI: 1.32 - 3.12), been diagnosed with a mental illness (PR = 2.58, 95% CI: 1.18 - 5.66), dealt drugs (PR = 2.52, 95% CI: 1.66 - 3.85) and been incarcerated (PR = 1.40, 95% CI: 1.29 – 2.80). Women involved in gangs were more likely to have reported a history of childhood sexual abuse (PR = 3.08, 95% CI: 1.15 - 8.27). These results suggest that a variety of adverse experiences in early life are associated with a subsequent increased risk of gang affiliation among youth who are street-involved. Primary prevention strategies aiming to avert gang initiation among high-risk youth should seek to address mental health issues, childhood abuse, and other traumatic experiences that are commonly experienced by this population.

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IS SMOKING TRANSMITTABLE? MODELING THE EVOLUTION OF SMOKING PREVALENCE IN OKLAHOMA USING A DETERMINISTIC TRANSMISSION DYNAMICS APPROACH. *Sydney Martinez, Helene Carabin (University of Oklahoma Health Sciences Center, Oklahoma City OK 73104)

Many behaviors associated with chronic diseases seem to spread throughout the population much like an infectious disease. Evidence shows that youth smoking initiation is highly influenced by the smoking behaviors of peers or parents. An age-structured deterministic transmission dynamics approach was taken to model the change in smoking prevalences in Oklahoma and to predict the relative effectiveness of alternative control strategies. Parameters of the model were estimated from survey data on smoking behavior in youth ages 14 to 17 and adults 18 to 25 for Oklahoma between 2005 and 2011. Only youth and young adults (14-25 years old) were assumed to be susceptible to start smoking, and young adults not smoking by the age of 26 were assumed to remain non-smokers for the rest of their lives. Smoking adults were assumed to be at risk of quitting smoking, and adults that had quit were assumed to be at risk for failing and returning to smoking. The model was verified using historical prevalence data. The model adequately predicted the peak prevalence of smoking (55%) which occurred prior to the 1964 Surgeon General's Report warning of the dangers of tobacco. Quit attempts were then included in the model, with 50% of smokers attempting to quit once per year with a 5% change of success. Under these conditions, the prevalence of smoking decreased to 25-30%, which is similar to the current prevalence of smoking in Oklahoma. By varying the rates of cessation attempts and successes, the model predicted the prevalence of smokers under different social conditions. Under different conditions, when 70% of adult smokers made two quit attempts per year with a 15% chance of success, the overall prevalences of smoking for adults and youth drastically declined to below 10%. Transmission dynamics modeling may also help explain smoking prevalence differences and determine the likelihood of becoming a smoker.

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SOFT DRINKS AND BEHAVIOR PROBLEMS AMONG FIVE-YEAR OLDS IN THE FRAGILE FAMILIES AND CHILD WELLBEING STUDY. *Shakira Suglia, Sara Solnick, David Hemenway (Columbia University, New York NY 10032)

Recent research suggests soda consumption is associated with aggression and depression among adolescents. However, this association has not been examined among younger children. We examine soda consumption and aggressive behaviors, attention problems and withdrawn behavior among five-year-old children in the Fragile Families and Child Wellbeing Study. Mothers reported the child's behaviors using the Child Behavior Checklist (CBCL) at age 5 and were asked to report how many servings of soda the child drinks on a typical day. In the sample of 2957 children, 52% were boys, 51% were African-American 43% consumed at least one serving of soda per day and 4% consumed 4 or more servings per day. In analyses adjusted for socio-demographic factors, consuming one (Beta 0.7 95% CI 0.1,1.4), two (1.8 95% CI 0.8,2.7), three (2.0 95% CI 0.6,3.4) or four or more (4.7 95% CI 3.2,6.1) servings was associated with higher aggressive behavior score compared to consuming no soda. Furthermore, those who consumed four or more soda servings had a 1.7 (95% CI 1.0,2.4) point higher score on attention problems and a 1.8 (95% CI 1.9) point higher withdrawn behavior score compared to those who consumed no soda. Future studies should explore potential mechanisms linking soda consumption and behavior among children.

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DYNAMICS OF SEXUAL DEBUT AND SUBSTANCE USE AMONG UNIVERSITY YOUTH FROM LEBANON. *Lilian Ghandour, Faysal El Kak, Rola Yasmine (American University of Beirut, Beirut Lebanon)

The present study used online survey data on the sexuality and sexual behaviors of private university students from Lebanon (N = 2543) who reported having had their first sexual experience (oral, anal, and/or vaginal sex) while using alcohol/drugs. About 11% (n = 104) of sexually active students (n = 943) used alcohol/drugs at sexual debut; no differences in mean age (17 years) of first-time sex were observed. Males, non-Arab foreigners, and those living independently were at least twice as likely have used substances at sex debut. Compared to the very religious, the somewhat to not-at-all religious or spiritual were 3.3 and 5.6 times as likely to report alcohol/drug use at sexual debut [p-value < 0.0001]. Similarly, students who attended a religious high school, always lived in Lebanon, and were in a relationship had 40-60% lesser odds to use substances during sex debut [p-values 0.004-0.019]. Sex debut under the influence placed youth at significantly higher odds of engaging in oral sex with an unfamiliar partner, even after controlling for gender, nationality, current relationship status, having lived abroad, and religiosity/spirituality [Odds ratio = 3.04, 95% CI = 1.7-5.2]. In contrast, the association with first-time vaginal sex with an unfamiliar partner faded when adjusted for sex (male). Interestingly, ever experiencing sexual abuse or coercion was not linked to substance abuse at debut, nor was the use of condoms and paying for sex. Study findings highlight the distinct demographic profile and cultural background of students who engaged in first-time sex while using alcohol/drugs. Moreover, it sheds light on the dynamics of sexual debut in an Arab country, highlighting the behaviors that are accessible (oral with unfamiliar partners) to all youth engaging in sexual debut under the influence versus males only (vaginal), perhaps given the patriarchal and/or conservative society that limits the expression of sexual desires.

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REDEFINING LIGHT AND INTERMITTENT SMOKERS USING U.S. NATIONAL HEALTH SURVEY DATA. *Carolyn Reyes-Guzman, Neil Caporaso (National Cancer Institute, Rockville MD 20852)

Background: Light and intermittent smokers (LITS) have been the fastest growing segment of smokers in the U.S. during the past 15 years. National survey data indicates the prevalence of nondaily smokers ranges from about 20% to nearly 40%. Defining the characteristics and health consequences for this behavior is an urgent priority. Researchers have used diverse definitions of LITS: Chippers, occasional smokers, some-day smokers, and light or very light smokers. It is likely however, that smokers who fall in these categories comprise a heterogeneous mix. In the proposed work we address the heterogeneity question in LITS using national survey data. We propose to create a factor structure from an empirically specified model of observed variables. Methods: We analyzed demographic and behavioral data from three U.S. population-based surveys: 2010 NHIS, 2010 NSDUH, and 2009-2010 NHANES. We plan to use nicotine-related biomarker data present in NHANES. A Confirmatory Factor Analysis model will be fit according to measures on demographics, smoking, and other behaviors, to obtain latent structures which separate LITS into "Casual Smokers" and "Forced Reducers" groups. Results: We will describe specific behavioral patterns that distinguish categories within LITS that we provisionally distinguish as "Casual" and "Forced". We will also describe how LITS differ from regular and heavy smokers. Conclusion: We will disaggregate the heterogeneity in LITS using an empirically-derived factor structure to establish an improved definition that can be adopted by other investigators. This newly created definition verifies whether the factor structure is better able to characterize LITS, or whether cigarettes per day and smoking duration are the best available measures in spite of their shortcomings. These findings can translate into preventive policies targeted at the two projected groups of LITS: "Forced Reducers" and "Casual Smokers".

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DENTAL CARIES AND ORAL HEALTH BEHAVIOURS IN A PORTUGUESE SAMPLE OF ADOLESCENTS. *Carlos Pereira, Nelio Veiga, Claudia Chaves, Paula Nelas, Odete Amaral, Ines Coelho, Ilidio Correia, Paula Ferreira, Eduardo Ferreira, Helena Morais, Manuela Ferreira (CI&DETS-Polytechnic Institute of Viseu; Beira Interior University; Health Science Department UCP; CPEFPRC-FCTUC; FHU Grao Vasco; Schools of Satao, Portugal)

Background: The frequency of toothbrushing, use of dental floss and regular dental appointments are important behaviours to prevent oral diseases. The objective of this study was to determine the mean of decayed/missing/filled in permanent teeth (DMFT index) and assess the oral health behaviours in a sample of adolescents. Participants and methods: A sample of 293 adolescents aged 12 to 18 years old, attending a public school in Satao, Portugal, was enrolled in this cross-sectional study. A self-administered questionnaire with questions about oral health behaviours and socio-economic status was answered by adolescents in the classroom. Clinical examination of oral health status was carried out according to the World Health Organization criteria to determine the prevalence of dental caries and the DMFT index. Results: The prevalence of toothbrushing (twice-a-day or more) was 78.2%, more frequent among the female gender (82.9% vs. 72.3%, p = 0.02). Four point one percent of adolescents reported daily flossing, more frequent among female gender (48.4% vs. 37.3%, p = 0.04). Sixty-two point five percent had a dental appointment once or more times in the previous twelve months and the most frequent reasons referred were: 74.3% for a dental check-up and 26.2% when having a toothache. The DMFT index was 3.26 and the prevalence of dental caries 40.1% associated with gender (male = 33.3% vs female = 45.5%, p = 0.03), parents' level of education (<4 yrs = 27.3%, 4-12 yrs = 44.7% and >12 yrs = 22.2%, p = 0.02) and fear of the dentist (no = 37.8% vs yes = 54.3%, p = 0.05). Conclusions: We found a moderate DMFT index and prevalence of dental caries. One forth of adolescents don't make a anual dental check-up appointment and visit a dentist only when they have toothache. Oral health community programs and primary preventive strategies should be considered in order to reduce a higher level of oral diseases and improve oral health behaviours.

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THE IMPACT OF CARDIAC AND NONCARDIAC COMORBIDITIES ON THE SHORT-TERM OUTCOMES OF PATIENTS HOSPITALIZED WITH ACUTE MYOCARDIAL INFARCTION: A POPULATION-BASED PERSPECTIVE. *Han-Yang Chen, Jane Saczynski, David McManus, Kate Lapane, Joel Gore, Robert Goldberg (University of Massachusetts Medical School, Worcester MA 01655)

Background: Coronary heart disease (CHD) is associated with a high burden of comorbidities that play a critical role in disease progression and treatment response. The objectives of our study were to describe the prevalence of cardiac (CAM) and noncardiac comorbidities (NonCAM) in a large community-based population of patients hospitalized with acute myocardial infarction (AMI) and to examine if multiple CAMs and NonCAMs were associated with worse hospital outcomes. Methods: Data from the Worcester Heart Attack Study were utilized (2003, 2005, 2007). Multivariable logistic regression analyses were used to examine the association between number of CAMs and NonCAMs (0, 1, 2, ≥3) and in-hospital case-fatality rates and hospital length of stay (LOS) (>3 vs. ≤3 days) while adjusting for several potential confounders. Comorbidities included atrial fibrillation, CHD, heart failure, hypertension, peripheral vascular disease, stroke, anemia, depression, diabetes, cancer, COPD, and renal disease. Results: The study sample included 2,972 patients hospitalized with AMI. The mean age of this population was 71 years; 45% were women, and 93% were white. Hypertension (75%) was the most common CAM while diabetes (35%) was the most common NonCAM in this population. One third of patients had ≥3 CAMs while 15% had ≥3 NonCAMs. Patients with ≥3 CAMs were more likely (OR = 2.2; 95% CI = 1.2, 4.2) to have died during hospitalization, and had a 57% increased odds of having a hospital LOS >3 days, compared with those with no CAM. Patients with ≥3 NonCAMs were more than twice as likely to have died during hospitalization or have a hospital LOS >3 days, compared with those with no NonCAM. Conclusions: Presence of multimorbidities was associated with worse hospital outcomes. Our findings highlight the need for additional contemporary data to help guide the use of effective treatment strategies for patients with AMI and multiple concurrent medical illnesses.

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SLEEP IMPAIRMENT AND PROGNOSIS OF ACUTE MYOCARDIAL INFARCTION: A PROSPECTIVE COHORT STUDY. *Alice Clark, Theis Lange, Johan Hallqvist, Poul Jennum, Naja Hulvej Rod (Department of Public Health, University of Copenhagen, Copenhagen Denmark)

Objective: Impaired sleep is an established risk factor for development of cardiovascular disease, while less is known about the effect on prognosis. The aim of this study is to determine how different aspects of impaired sleep affect short- and long-term prognosis in patients with an acute myocardial infarction (AMI). Methods: The Stockholm Heart Epidemiology Program included 2,246 persons with first-time AMI. Recall of disturbed sleep, impaired awakening, daytime sleepiness, and nightmares was assessed by the Karolina Sleep Questionnaire. Case fatality, defined as death within 28 days of initial AMI, and new cardiovascular events were identified through national registries within a 10-year follow-up. Information from a physical examination and a comprehensive questionnaire enabled thorough adjustment for confounders. Results: In women, disturbed sleep showed consistent effects on long-term prognosis, with a higher risk of all assessed cardiovascular events: AMI (hazard ratio = 1.69; 95% confidence interval 0.95-3.00), stroke (HR = 2.61; 95% CI 1.19-5.76), and heart failure (HR = 2.43; 95% CI 1.18-4.97), while no clear effects was found for case fatality. In men, only small, if any, effects were indicated between impaired sleep and long-term prognosis. Meanwhile, a strong short-term effect on case fatality (HR = 3.27; 95% CI 1.76-6.06) was observed in men with impaired awakenings. Further, while the index of daytime sleepiness was not associated with the risk of case fatality, two of the items i.e. feeling sleepy during the day and involuntary sleep episodes in leisure time were associated with twice the risk of case fatality in men. Conclusion: Results suggest gender-specific effects of impaired sleep that differ by short and long-term prognosis. Sleep complaints are frequent, easily recognizable, and potentially manageable for most patients and evaluation of sleep complaints may, even if they represent prognostic markers rather than risk factors, provide additional information in clinical risk assessment that could benefit secondary cardiovascular prevention.

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COMPARISON OF COMPLIANCE WITH JOINT COMMISSION MEASURES IN STATE DESIGNATED COMPREHENSIVE VS. PRIMARY STROKE CENTERS. Spozhmy Panezai MD, *Tefera Gezmu, Florence Chukwuneke, Ratna Bitra, Martin Gizzi (Rutgers, The State University of New Jersey, New Brunswick NJ 08901)

Background: Comparisons of state designated Primary (PSCs) and Comprehensive Stroke Centers (CSCs) with regard to adherence to nationally accepted performance standards are scarce. The objective of this study was to examine if significant association exists between level of designation and fulfillment of Joint-Commission core measures. Methods: A retrospective comparative data analysis of the New Jersey acute stroke registry for the calendar years 2010 and 2011. Joint Commission (JC) core measures were compared by hospital level (PSCs vs. CSCs). Adjusted odds ratios (aOR) were estimated for the association between hospital levels and fulfillment of JC core measures. Median door to thrombolytic time was also compared. Results: There were 39, 751 acute stroke admissions in the registry. More patients were admitted at PSCs than CSCs (57% and 43%, respectively). Hemorrhagic stroke admissions at were 2.5 times larger at CSCs than PSCs (19.1% and 7.4%, respectively). PSCs were less likely to meet the JC compliance measures. Overall, 16.9% of eligible patients received thrombolytic therapy at CSCs compared to 9.4% at PSCs, with a 44% difference in the provision of thrombolytic therapy. (aOR = 0.52, 95% CI 0.46-0.59). Stroke education was more likely to be provided at PSCs compared to CSCs, with a minimal difference of about 2% (aOR = 1.7, 95% CI; 1.3-2.23); and the median doors to thrombolytic drug times were significantly shorter at CSCs compared to PSCs (65.0 versus 74.0 minutes, $p < 0.0001$). Conclusions: In New Jersey, state-designation as a CSC is associated with a slightly greater compliance with the JC core stroke measures and shorter door to thrombolytic drug times. This may translate into better stroke care for patients treated at CSCs.

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MORTALITY AND THE RISK OF CARDIOVASCULAR EVENTS IN BARRETT'S ESOPHAGUS. *Jennifer Lund, Rune Erichsen, Erzsebet Horvath-Puho, Lars Pedersen, George Davey-Smith, Henrik Toft Sorensen (Aarhus University, Aarhus Denmark)

Individuals diagnosed with Barrett's esophagus (BE) are at increased risk of developing esophageal cancer. However, the impact of BE on mortality remains unclear. Controversy exists regarding cardiovascular-specific mortality in BE; yet, no studies have examined the risk of cardiovascular events. We examined the association between BE and overall mortality and the risk of acute myocardial infarction (MI), subarachnoid hemorrhage (SAH), hemorrhagic stroke, ischemic stroke, venous thromboembolism (VTE), and heart failure using Danish population-based medical registries. We conducted a nationwide matched cohort study including all adults with histologically verified BE from 2005-2011 (n = 7,576) and a comparison cohort matched on age, sex, individual Charlson comorbidities, and calendar time (n = 69,045), free from study endpoints at BE diagnosis or matched index date. We computed overall mortality rates (median follow-up= 3 years) and estimated adjusted hazard ratios (aHR) and 95% confidence intervals (CIs) using Cox proportional hazards regression for each endpoint, adjusting for prior medication use and other comorbidities. There were 1,063 deaths in BE patients (46/1,000 person-years) and 4,816 deaths in the comparison cohort (22/1,000 person-years) during follow-up (aHR = 2.0, 95% CI: 1.8, 2.1). The risk of ischemic (aHR = 1.5, 95% CI: 1.2, 1.7) and hemorrhagic (aHR = 1.4, 95% CI: 1.0, 2.1) stroke and VTE (aHR = 2.0, 95% CI: 1.6, 2.4) were elevated in BE patients. There was no association between BE and the risk of MI, SAH, or heart failure. Overall mortality and the risk of selected cardiovascular events were higher in BE patients compared to similar individuals without BE. Shared lifestyle factors for BE and cardiovascular disease may partly explain these findings.

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CROSS-SECTIONAL STUDY OF THE PREDICTORS OF MEDICATION USE, HYPERTENSION PREVALENCE, AND HYPERTENSION TREATMENT IN BANGLADESHI ADULTS. *Molly Scannell, Maria Argos, Brandon Pierce, Faruque Parvez, Alauddin Ahmed, Habibul Ahsan (University of Chicago, Chicago IL 60637)

Background: Medication use for chronic conditions is not well characterized in South Asian populations. Additionally, patient characteristics that predict hypertension and its proper treatment have not been explored in a population-based study. Objectives: Utilize data from the population-based Health Effects of Arsenic Longitudinal Study (HEALS) to evaluate the predictors of medication use. Additional analyses will be presented on the prevalence and predictors of treatment for hypertension. Design: The 20,033 participants of the HEALS study in Araihazar, Bangladesh provided information at baseline about demographics, environmental exposures, medical history, and medicine use. Logistic regression models estimated odds ratios and 95% confidence intervals. Predictors of hormonal contraception use, and medications that treat chronic cardiovascular, mental health, and respiratory disease were assessed. Logistic regression was also used to assess both the predictors of hypertension, and the predictors of appropriate pharmaceutical treatment for hypertension. Results: Age, gender, marital status, religion, education, socioeconomic status, smoking, exposure to arsenic, and weight predict use of each of the medication classes. Among those with hypertension (13.5%), 1.5% were on anti hypertensive medications at baseline. Increasing age and education is associated with increased use of hypertension medications, as is being a past smoker, Hindu religion, owning land, and owning a TV. Being underweight is associated with decreased use of hypertension medications. Conclusion: This analysis gives an estimate for population levels of medication use in rural Bangladesh, and demonstrates the gap between those with hypertension and those who receive proper treatment for it. The analysis also suggests which factors predict treatment, suggesting who may be targeted for public health interventions.

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ASSESSING HETEROGENEITY OF EFFECTS ON BLOOD PRESSURE IN A META-ANALYSIS OF PHARMACIST INTERVENTIONS TRIALS.

Arnaud Chiolero, Bernard Burnand, Robert Platt, Gilles Paradis, *Valérie Santschi (University of Lausanne & McGill University, Switzerland & Canada)

Background: Recent reviews of randomized control trials have shown that pharmacist interventions improve cardiovascular diseases (CVD) risk factors in outpatients. Various interventions were evaluated in different settings, and a substantial heterogeneity was observed in the effect estimates. To better express uncertainties in the effect estimates, prediction intervals (PI) have been proposed but are, however, rarely reported. Objective: Pooling data from two systematic reviews, we estimated the effect of pharmacist interventions on systolic blood pressure (BP), computed PI, and evaluated potential causes of heterogeneity. Methods: Data were pooled from systematic reviews assessing the effect of pharmacist interventions on CVD risk factors in patients with or without diabetes, respectively. Effects were estimated using random effect models. Results: Systolic BP was the outcome in 31 trials including 12 373 patients. Pharmacist interventions included patient educational interventions, patient-reminder systems, measurement of BP, medication management and feedback to physician, or educational intervention to health care professionals. Pharmacist interventions were associated with a large reduction in systolic BP (-7.5 mmHg; 95% CI: -9.0 to -5.9). There was a substantial heterogeneity (I2: 66%). The 95% PI ranged from -13.9 to -1.0 mmHg. The effect tended to be larger if the intervention was conducted in a community pharmacy and if the pharmacist intervened at least monthly. Conclusion: On average, the effect of pharmacist interventions on BP was substantial. However, the wide PI suggests that the effect differed between interventions, with some having modest effects and others very large effects on BP. Part of the heterogeneity could be due to differences in the setting and in the frequency of the interventions.

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SMOKING AND HEMORRHAGIC STROKE MORTALITY IN A PROSPECTIVE COHORT STUDY OF OLDER CHINESE.

*Lin Xu, C Mary Schooling, Wai Man Chan, Siu Yin Lee, Tai Hing Lam, Gabriel M Leung (University of Hong Kong, Hong Kong SAR China)

Objective: Hemorrhagic stroke is relatively more common in non-Western settings and does not always share risk factors with other cardiovascular diseases. The role of cigarette smoking in most types of stroke is well established except for hemorrhagic stroke. We examined the association of cigarette smoking with hemorrhagic stroke, including intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH), in a large cohort of older Chinese from Hong Kong. Methods: Multivariable Cox regression analysis was used to assess the adjusted associations of smoking at baseline with death from hemorrhagic stroke, using a population-based prospective cohort of 66,820 Chinese aged 65+ years enrolled from July 1998 to December 2001 at all the 18 Elderly Health Centers of the Hong Kong Government Department of Health, and followed until May 31, 2012. Results: After follow up for an average of 10.9 years (standard deviation = 3.1), 648 deaths from hemorrhagic stroke had occurred, of which 530 (82%) were ICH. Current smoking was associated with a higher risk of hemorrhagic stroke (hazard ratio 2.19, 95% confidence interval 1.49-3.22), ICH (1.94, 1.25-3.01) and SAH (3.58, 1.62-7.94), adjusted for age, sex education, public assistance, housing type, monthly expenditure, alcohol use and exercise. Further adjustment for hypertension and body mass index little changed the estimates. Conclusion: Smoking is strongly associated with hemorrhagic stroke mortality particularly for subarachnoid hemorrhage.

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MODEL SELECTION FOR PEDIATRIC CORONARY DIAMETER CURVES IN JAPAN BY RELATIVE GOODNESS OF FIT.

Shigeto Fuse, Tohru Kobayashi, Yoshio Arakaki, Shunichi Ogawa, Hitoshi Katoh, Kenji Hamaoka, Tsutomu Saji, *Naoko Sakamoto (National Research Institute for Child Health and Development., Japan)

Introduction: The Z score project began in May 2010 as an effort to develop a Pediatric Coronary Diameter Z score Calculator, which could be used to easily and quickly compute coronary diameter Z scores. Participants in the project, who included children without pre-existing diseases, were asked to register the following data left main coronary (LM) artery, left anterior descending (LAD) artery, left circumflex (LCX) artery, right coronary artery (RCA), age, sex, height, and weight. Although the estimated necessary sample size for the Z score project was 4000 from the simulation, valid data has been collected on 4533 children as of December 2011. The objective of this study was to select models for pediatric coronary diameter curves in Japan. Methods: We analyzed the data with the LMS method, using age, height, and body surface area (BSA). BSA was calculated by the Du Bois expression and the Haycock expression (BSA d and BSA h, respectively). We compared the relative goodness of fit of these models using Akaike's information criterion (AIC), generalized AIC (GAIC), and Schwarz Bayesian Criteria (SBC), for the whole 4533 data and the sub data set including 1931 cases whose BSA d were below 0.7. Results: All criterions revealed the age and the height models to be poorer in predicting coronary diameters in the pediatric population in the whole data analysis. Additionally, the goodness of fit of the BSA d and BSA h models were quite similar, for all arteries. According to the sub data results, the goodness of fit of the BSA h models was slightly better than the BSA d model. Conclusions: The BSA d and BSA h models were better at predicting pediatric coronary diameter by comparison to the age or height models. Although BSA estimation by the Du Bois expression is quite popular in Japan, it would be better to develop the Pediatric Coronary Diameter Z score Calculator using BSA by the Haycock expression.

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SUBCLINICAL ATHEROSCLEROSIS AND PSORIASIS.

Henrique Staniak, Cid Sabbag, Marcio Bittencourt, Rodolfo Sharovski, Angelita Souza, *Paulo Lotufo, Isabela Bensenor (University of Sao Paulo, Sao Paulo SP Brazil)

Background: Psoriasis is a common inflammatory disease that affects the skin and joints. Recent evidence suggests that frequency of cardiovascular disease is higher among patients with psoriasis than to people free of disease. Our aim is to compare calcium score (CAC) in subjects with and without psoriasis. Methods: a cross-sectional analysis that included 232 patients with diagnosis of psoriasis and 660 controls paired by sex and age (5-year interval). All participants answered a questionnaire about cardiovascular risk factors, and they were submitted to an oral glucose tolerance test, and HDL, LDL-cholesterol, triglycerides and us-CRP determinations. CAC was measured using a CT-scan Philips Brilliance 64. Results: Mean (standard deviation) age was 56.7 (7.6) and 57.2 (7.0) respectively for subjects with and without psoriasis. Patients with psoriasis had a higher frequency of diabetes (30.8% vs. 18.3%; $P < 0.0001$), higher levels of triglycerides (39.4% vs. 30.0%; $P < 0.0001$), and lower levels of HDL-cholesterol (38.0% vs. 20.4%; $P < 0.0001$); however, they present lower levels of LDL-cholesterol (34.4% vs. 48.7%; $P < 0.0001$) compared to controls; as expected, levels of high sensitivity-CRP were higher in subjects with psoriasis compared to controls (4.3 (5.3) vs. 2.8 (4.2); $P < 0.0001$). The frequency of coronary calcification (CAC > 400 Agatston) was higher in subjects (9.1%) with disease than controls (5.3%) ($P = 0.03$). Subjects with psoriasis present an odds ratio of 1.78 (95% confidence interval: 1.02-3.13) coronary calcification compared to controls. Concluding, patients with psoriasis have a higher frequency of coronary calcification and of risk factors compared to people free of disease.

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ANXIETY AND ANGER AND MORTALITY AMONG EARLY SURVIVORS OF ACUTE MYOCARDIAL INFARCTION.

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Background: Although there is relatively consistent evidence that anxiety and anger are associated with increased risk of incident cardiovascular events, studies examining the relationship between psychosocial stressors and prognosis following acute myocardial infarction (MI) have been mixed. Methods: We conducted a prospective cohort study of 1985 participants (30.5% women) in the Determinants of Myocardial Infarction Onset Study recruited at the time of admission for acute MI between 1989 and 1994. We used the state anxiety and anger subscales of the State-Trait Personality Inventory, with a level above the 90th percentile classified as high exposure. Participants were followed for all-cause mortality through December 31, 2007 using the National Death Index. We constructed multivariable Cox proportional hazards models adjusted for demographic, behavioral, and clinical confounders and calculated hazard ratios (HR) and 95% confidence intervals (CI) to examine the relationship between high levels of anxiety and anger and all-cause mortality. Results: Over 10 years of follow-up, 525 participants died. Compared to those scoring low, a high score on the anxiety scale was associated with a 1.28-times (95% CI 0.91-1.79) higher mortality rate over 10 years. The association was apparent in the first 3 years (HR = 1.79; 95% CI 1.09-2.92), but not thereafter (HR = 1.00; 95% CI 0.63-1.60). Likewise, scoring high on the anger scale was associated with a 1.27-times (95% CI 0.90-1.80) higher mortality rate over 10 years. The hazard ratio was higher in the first 3 years (HR = 1.56; 95% CI 0.90-2.71) than in subsequent years (HR = 1.13; 95% CI 0.72-1.78). Conclusions: In this study of MI survivors, high levels of anxiety and anger were associated with all-cause mortality, with the strongest association in the first 3 years of follow-up.

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STROKE AFTER ANTIPSYCHOTIC USE AND THE CAUSAL PATHWAY TO DEATH IN OLDER ADULTS.

*John W Jackson, Tyler J VanderWeele, Deborah Blacker, Sebastian Schneeweiss (Harvard School of Public Health, Boston MA 02115)

Objective: To quantify how much stroke contributes to the difference in mortality between first-generation (FGAs) and second-generation (FGAs) antipsychotic agents. Study Design: A cohort of elderly 9,885 FGA and 21,228 SGA new users, who were concurrently enrolled in statewide pharmacy assistance programs in New Jersey or Pennsylvania Medicare, were followed for incident ischemic or hemorrhagic stroke until death, for up to 6 months after antipsychotic initiation. We estimated direct and indirect effects of antipsychotic type on mortality through stroke using the risk ratio scale; we also calculated the percent of the difference in mortality mediated by stroke using the risk difference scale. Results: FGAs showed marginally higher risk for stroke (risk ratio [RR] = 1.18; 95% confidence interval [CI] 0.93, 1.50) and mortality (RR = 1.14; 95% CI 1.06, 1.23) as compared to SGAs, but stroke explained little (2.7%) of the observed difference in mortality. The indirect effect was null (RR = 1.00; 95% CI 1.00, 1.01), and the direct effect was similar to the total effect of antipsychotic type (FGA vs. SGA) on mortality (RR = 1.15; 95% CI 1.09, 1.22). Conclusions: These results suggest that the difference in mortality between FGA and SGA users develops mostly through pathways that do not involve stroke. Studies with better stroke and confounder ascertainment would help confirm this finding.
Keywords: antipsychotic, mortality, stroke, cerebrovascular event, adverse event, mediation analysis, direct effect, indirect effect, proportion mediated, causal inference

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PROGNOSIS AFTER ISCHEMIC HEART DISEASE ACCORDING TO BODY SIZE: A COHORT STUDY.

*Christina C Dahm, Anders Helles Carlsen, Anne Tjønneland, Thorkild IA Sørensen, Kim Overvad (Aarhus University, Aarhus Denmark)

Background: Among incident cases of ischemic heart disease, overweight or mildly obese patients experience lower mortality than patients of normal or low weight or those who are very obese. This may reflect differing associations of lean and fat mass with mortality. Here, we investigate associations between pre-diagnostic body mass index (BMI), waist circumference (WC), fat and lean body mass indices and mortality among incident cases of ischemic heart disease. Methods: The Danish cohort study Diet, Cancer and Health consists of 57,053 men and women aged 50-64 at recruitment (1993-1997), when data on anthropometry, bioelectrical impedance and potential confounders were collected in study clinics. Incident ischemic heart disease status, obtained by linkage to national registers, was designated as entry time to this study, and failure as death or censoring. Centred restricted cubic splines of body size and composition measures of cases were related to mortality using Cox proportional hazards models adjusted for potential confounders. Results: 2356 incident cases were included, recruited 4 months-12 years prior. Hazards of death were greater for cases of BMI <23 kg/m2 and >31 kg/m2 compared to cases of median BMI (26.9 kg/m2), and did not level off at still greater body mass indices. Greater hazards of death were observed for those of low BMI for given WC or of low fat mass index, compared to median measures. However, cases of either very low or very high lean mass indices experienced greater hazards of death, compared to the median. Large, but not small, WC were associated with greater hazard of dying, compared to the median. Nevertheless, when WC was adjusted for BMI, the association was linear and positive (hazard ratio = 1.03, 95% confidence interval 1.01; 1.04 per cm). This study indicates that among ischemic heart disease cases, having a trim waist and average muscle mass prior to incident disease are related to the best chance of survival afterwards.

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NURSING EDUCATIONAL INTERVENTIONS IN OUTPATIENTS WITH HEART FAILURE.

*Wilson Canon-Montanez (Post Graduate Program in Epidemiology, Universidade Federal do Rio Grande do Sul, Porto Alegre Rio Grande do Sul Brazil)

Introduction: The number of patients with heart failure is increasing. The aim of this study was to determine the efficacy of two nursing educational strategies to raise the knowledge about the disease in outpatients with heart failure. Methods: Randomized clinical trial. Two nursing strategies intervention were implemented: personalized education and education by phone. Each group was randomly to receive 3 intervention sessions with duration of 30 minutes and a frequency of two weeks between each session. The main outcome was evaluated by two independent assessors. The nurse who performed the interventions did not know the results of the evaluations of patients. Furthermore, the researcher who conducted the data analysis and the assessors of the main outcome were blinded to the intervention groups. Subjects were recruited from the cardiology outpatient service of the University Hospital from Santander-Colombia. Analysis was by intention to treat. Results: 116 outpatients were randomized, 58 were assigned to personalized education and 58 to education by phone. In the group who received personalized education, the delta score of knowledge increased in the final evaluation at 1.04 (95% CI: 0.94, 1.14), and in the follow up at 0.73 (95% CI: 0.63, 0.83). Also, for the group assigned to education by phone, the delta score of knowledge increased in the final evaluation at 1.00 (95% CI: 0.92, 1.07), and in the follow up at 0.73 (95% CI: 0.64, 0.81). Conclusions: In this study was not shown that personalized education is more effective than education by phone. Both interventions had a beneficial effect. Nursing education in these patients, regardless of the strategy (personalized or by phone) is useful and therefore nurses should be included in the multidisciplinary teams of care. (Latin American Clinical Trials Register: COL112).

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HYPERTENSIVE DISORDERS IN PREGNANCY AND RISK OF MYOCARDIAL INFARCTION AND STROKE. *Jennifer J Stuart, Eric B Rimm, Stacey A Missmer, Donna Spiegelman, Eileen N Hibert, Kathryn M Rexrode, Kenneth J Mukamal, Janet W Rich-Edwards (Harvard School of Public Health, Boston MA 02120)

Background: Women with a history of hypertensive disorders in pregnancy appear to have a two-fold increased risk of myocardial infarction (MI); the few studies on stroke suggest similar associations. However, reported associations remain largely uncontrolled for key pre-pregnancy variables, including body mass index (BMI) and family history. The aim of this study was to examine the association between hypertensive disorders in pregnancy and MI and stroke in the Nurses' Health Study II (NHSII). Methods: NHSII participants reported hypertensive disorders in pregnancy at baseline in 1989 and biennially until 2001. Mothers of singleton live births who provided pregnancy history in 2001 and were free of MI and stroke at baseline comprised the study sample. Women were followed for non-fatal and fatal MI and stroke through 2009. Cox proportional hazards models estimated hazard ratios (HR) and 95% confidence intervals (CI) for MI and stroke among women with a history of preeclampsia or gestational hypertension. Models adjusted for age, race, parental history of MI < 60, and pre-pregnancy smoking and BMI. Results: Among 53,003 women, 14% reported ever experiencing a hypertensive disorder in pregnancy. Over 1,098,193 person-years of follow-up, we identified 287 incident cases of MI and 274 of stroke. Compared to normotensives, history of preeclampsia was associated with an age-adjusted HR of 1.9 (CI: 1.4, 2.5) for MI and 1.9 (CI: 1.4, 2.6) for stroke. After multivariate adjustment, women with a history of preeclampsia had a 1.6-fold increased risk of MI (CI: 1.2, 2.2) and 1.8-fold increased risk of stroke (CI: 1.3, 2.4). An increased risk was observed with history of gestational hypertension but associations were not statistically significant. Conclusion: These findings suggest history of preeclampsia identifies women at increased risk for both MI and stroke. Research is needed to evaluate if this information may be used to prevent future cardiovascular events.

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WEIGHT-OF-EVIDENCE EVALUATION OF THE CARDIOVASCULAR EFFECTS OF OZONE EXPOSURE. *Heather Lynch, Sonja Sax, Robyn Prueitt, Julie Goodman (Gradient, Cambridge MA 02138)

There is a considerable body of research on the cardiovascular (CV) effects associated with ozone exposure, including epidemiology, toxicology, and controlled human exposure studies. US EPA is considering these data to determine whether to update the ozone National Ambient Air Quality Standards (NAAQS). We conducted a weight-of-evidence (WoE) analysis to determine if there was an association between CV effects and ozone at levels below the current primary ozone NAAQS, which is currently set at 75 parts per billion. The epidemiology evidence of CV morbidity and mortality is inconsistent and lacks coherence among specific CV endpoints. Toxicology studies are conducted at very high exposure levels with little relevance to ambient human exposures. Furthermore, there is a lack of coherence between reported results from epidemiology studies (suggesting no effects) and results from animal studies (suggesting small, but inconsistent, effects at high exposure levels). Similarly, human exposure studies report only small effects at levels above the current NAAQS. Overall, the WoE analysis indicates that CV effects are not associated with ozone exposures below the current NAAQS

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SHORT-TERM EFFECT OF DUST STORMS ON THE RISK OF MORTALITY DUE TO RESPIRATORY, CARDIOVASCULAR AND ALL-CAUSES IN KUWAIT. *Abdullah Al-Taiar, Lukman Thalib (Faculty of Medicine, Kuwait University, Kuwait)

The study aimed to investigate the impact of dust storms on short-term mortality in Kuwait. We analyzed respiratory and cardiovascular mortality as well as all- cause mortality in relation to dust storm events over a five-year study period, using data obtained through a population-based retrospective ecological time series study. Dust storms days were identified when the national daily average of PM10 exceeded 200 μg/m3. Generalized Additive Models with Poisson link were used to estimate the Relative Risk (RR) of age-stratified daily mortality associated with dust events, after adjusting for potential confounders including weather variables and long-term trends. There was no significant association between dust storm events and same-day respiratory mortality (RR = 0.96; 95% CI: 0.88-1.04), cardiovascular mortality (RR = 0.98; 95% CI: 0.96-1.012) or all-cause mortality (RR = 0.99; 95% CI: 0.97-1.00). Overall our findings suggest that local dust, that most likely originates from crustal materials, has little impact on short-term respiratory, cardiovascular or all-cause mortality.

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POLYFLUOROALKYL CHEMICALS AND NATURAL MENOPAUSE AMONG WOMEN AGES 18-65 FROM NHANES 1999-2000, 2003-2004, 2005-2006, 2007-2008, AND 2009-2010. *Kyla Taylor, Kate Hoffman, Kristina Thayer, Julie Daniels (University of North Carolina- Chapel Hill; National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park NC 27709)

Polyfluoroalkyl chemicals (PFCs) have been associated with early menopause onset; however, previous cross sectional studies have not had adequate data to investigate the possibility of reverse causality. We investigate the association between perfluorooctane sulfonate (PFOS), perfluorooctanate (PFOA), perfluorononanoate (PFNA), and perfluorohexane sulfonate (PFHxS) and age at natural menopause in the National Health and Nutrition Examination Survey (NHANES). PFCs were assessed in 3600 women ages 18-65 (NHANES1999-2000 and annually 2003-2010). Using proportional hazard modeling, we assessed the rate of the onset of natural menopause as a function of age and PFC levels. Additionally we investigated the possibility of reverse causation by assessing the rate of hysterectomy, we also used multiple regression to determine whether time since menopause predicted PFC levels. After adjusting for age at survey, race/ethnicity, education, ever smoking, and parity, and accounting for NHANES sampling design, women with higher levels of PFCs had higher rates of earlier menopause compared to women with the lowest levels. For example, we observed a positive dose-response association between rate of menopause and level of PFHxS with a hazard ratio of 1.47 (95% confidence interval: 1.14, 1.90). However, we also found evidence of reverse causation: There was a positive association between rate of hysterectomy and PFCs and in a sensitivity analysis we found that that time since menopause strongly predicted serum PFCs. Overall our findings suggest that there is a relationship between PFCs and menopause; however, at least part of the association may be due to reverse causation. Causal or not, women appear to accumulate PFCs more rapidly after they are no longer menstruating, potentially increasing their risk of adverse health outcome associated with PFCs.

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NEIGHBORHOOD SELF-SELECTION: THE ROLE OF PRE-MOVE HEALTH STATUS ON THE POST-MOVE BUILT ENVIRONMENT.

*Peter James, Jaime Hart, SV Subramanian (Harvard School of Public Health, Cambridge MA 02138)

Background: Features of the built environment, such as urban sprawl, have been associated with physical activity and obesity. A criticism of this literature is the concept of confounding by 'residential self-selection,' implying that individuals select neighborhoods by pre-existing health preferences. Aim: To estimate the magnitude of residential self-selection by analyzing pre-move health factors and the post-move built environment. Methods: We used 1986-2008 data from the Nurses' Health Study, a nationwide prospective cohort. Our exposure was pre-move body mass index (BMI) (kg/m2) and metabolic equivalent hours of walking per week. Our outcome was post-move county sprawl index, a standardized measure based on residential density and street accessibility from the 2000 Census. We assigned the sprawl index to each nurse based on her biennial geocoded county of residence. We conducted linear regression with each change of county as the unit of analysis. Results: There were 13,083 county moves over follow-up. Participants were all female, 94% white, and had a mean age of 64 years. The highest tertile of pre-move BMI was associated with a 1.07 (95% Confidence Interval 0.35, 1.80) lower post-move sprawl index and the highest tertile of pre-move walking was associated with a 0.84 (0.12, 1.55) lower post-move sprawl index. Based on a mean sprawl index value of 104.7 and a standard deviation of 17.3, this demonstrates a weak association between pre-move health behaviors and the post-move built environment. Conclusions: We found little evidence of residential self-selection for the built environment in this population.

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IS THE ASSOCIATION BETWEEN AIR POLLUTANTS AND BIRTH WEIGHT CONSISTENT WITH USING DIFFERENT BUFFER SIZES?

*Keita Ebisu, Kathleen Belanger, Michelle Bell (Yale University, School of Forestry and Environmental Studies, New Haven CT 06511)

Numerous papers reported associations between fine particulate matter ($PM_{2.5}$) and birth weight, but few have investigated these effects for $PM_{2.5}$'s chemical composition. Spatial heterogeneity, which varies by pollutant, and associated exposure misclassification is a key challenge. We investigated associations between birth weight and $PM_{2.5}$ chemical components and gaseous pollutants, considering issues of buffer size. We used birth certificate data from Connecticut, U.S.A. (2000-2006), and ambient monitoring data of CO, NO_2, SO_2, particulate matter with aerodynamic diameter <10 μm (PM_{10}), $PM_{2.5}$, and $PM_{2.5}$ chemical components. We estimated the association between each pollutant and birth weight using seven different buffer sizes from 5 to 50km. Gestational exposure to NO_2, SO_2, PM_{10}, and $PM_{2.5}$ were associated with lower birth weight with any buffer size. For example, an interquartile range (IQR) increase in $PM_{2.5}$ was associated with lower birth weight by -9.8g [95% CI = -12.1, -7.5] with 50km buffer size. On the other hand, several pollutants show inconsistent results across different buffer sizes. For instance, IQR increase of $PM_{2.5}$ sulfate did not show association with 5km buffer (1.9g [-58.6, 62.4]), while it showed a statistically significant association with 50km buffer (-12.4g [-17.7, -7.1]). Results indicate there are associations between several air pollutants and birth weight, and that some $PM_{2.5}$ chemical components appear more harmful than others. Effect estimates vary with different buffer sizes, implying that there is a possibility for exposure misclassification. Homogeneous pollutant levels within a certain distance or geographic unit is a basic assumption in many environmental epidemiology studies, but our findings suggest that different exposure metrics may be needed for different pollutants.

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ACUTE AIR POLLUTANT EXPOSURE AND BLOOD PRESSURE AT LABOR/DELIVERY ADMISSION.

*Tuija Männistö, Pauline Mendola, Kira Leishear, Danping Liu, Rajeshwari Sundaram (National Institutes of Health, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Rockville MD 20852)

Particulate matter (PM10 and PM2.5), ozone and nitrogen oxides (NOx) increase blood pressure (BP) acutely in the general population but the associations are unstudied in pregnancy. We studied a stratified random sample (n = 500) of women with singleton pregnancies in the Consortium on Safe Labor (2002-2008) including 249 normotensive women, 191 with hypertensive disorders of pregnancy and 60 with chronic hypertension. Clinical BP was measured at admission to labor/delivery (time 0) and hourly exposure to pollutants in the preceding day was obtained from Community Multiscale Air Quality models, yielding time lags from 0 to 24 hours. Linear regression estimated the effect of hourly air pollutants at each lag time on systolic and diastolic BP after adjustment for age, race/ethnicity, parity, smoking, insurance status, labor type (spontaneous, induced or pre-labor cesarean section) and time of day. Acute exposure to PM10, and benzene increased systolic BP and exposure to PM2.5, sulfur dioxide (SO2), anthracene and phenanthrene increased both systolic and diastolic BP among women with chronic hypertension (lags 0-4 for PM10, 0-17 for PM2.5, 0-4 for SO2, 0-3 for anthracene, lag 1 for benzene, and lags 0-3 for phenanthrene). The effect size peaked at lags of 0-1 hours. Ozone increased diastolic BP in normotensive women only (lags 0-1 and 23-24). In women with hypertensive disorders of pregnancy, exposure to 1,3-butadiene and styrene increased diastolic BP (lags 16-24), but carbon particles, NOx, benz[a]anthracene, benzene, nitrosamine, propene and toluene decreased systolic BP (lags 15-24). Acute air pollution exposure was associated with increases in BP at labor/delivery admission mainly in women with chronic hypertension.

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ASSOCIATION BETWEEN VAPOR INTRUSION AND HUMAN EXPOSURE TO TRICHLOROETHYLENE.

*Natalie Archer, Carrie Bradford, John Villanacci, Neil Crane, Richard Corsi, David Chambers, Benjamin Blount (Texas Department of State Health Services, Austin TX 78714)

Trichloroethylene (TCE) is a volatile organic compound that is a human carcinogen and can cause other adverse health effects. TCE groundwater plumes have been identified in three areas in Grand Prairie, Texas. Due to the potential for human exposure to TCE in indoor air through vapor intrusion, the Texas Department of State Health Services led an exposure investigation in Grand Prairie. The objective was to further understand the TCE vapor intrusion pathway and its association with human exposures. Indoor air, outdoor air, soil gas, and tap water samples were collected in and around 36 randomly selected homes in 4 neighborhoods in Grand Prairie, and blood and urine samples were collected from 63 residents in these homes. Environmental and blood samples were analyzed for TCE and urine samples were analyzed for trichloroacetic acid (a metabolite of TCE). Mixed model multiple linear regression analyses were performed to determine associations between environmental levels of TCE (in indoor air, outdoor air, and soil gas) and levels of TCE in residents' blood. Reportable blood TCE levels were present in 17.5% of participants' blood samples. Indoor air, outdoor air, and soil gas TCE levels above the detect limit were present in 54.3%, 47.2%, and >84% of sampled homes, respectively. Both indoor air and soil gas TCE levels were significantly positively associated with participants' blood TCE levels ($p = 0.0002$ and $p = 0.043$). Geometric mean blood TCE levels of residents living in homes with indoor air TCE levels of >1.6 $\mu g/m^3$ (the 95th percentile for background indoor air levels) were approximately 50 times higher than geometric mean blood TCE levels in participants living in homes with no detectable TCE in their indoor air ($p < .0001$; 95% confidence interval 10.4 – 236.4). Results show evidence of a vapor intrusion pathway. Measuring TCE in soil gas or indoor air could be useful in predicting human exposure to TCE through vapor intrusion.

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FLUORIDE EXPOSURE IN DRINKING WATER AND CHILDHOOD AND ADOLESCENT OSTEOSARCOMA IN TEXAS. *Natalie Archer, John Villanacci, Tom Napier (Texas Department of State Health Services, Austin TX 78714)

Several studies to date have examined the relationship between fluoride in drinking water and risk of childhood osteosarcoma; however, results have been controversial. The purpose of this study was to examine the association between fluoride levels in drinking water and osteosarcoma among children and adolescents in Texas. We were able to examine a wide range of fluoride levels in drinking water because Texas has areas with both high and low naturally-occurring fluoride, as well as areas that optimally fluoridate. This was a population-based case-control study, with both cases and controls obtained from the Texas Cancer Registry. Eligible cases were Texas children and adolescents <20 years old who were diagnosed with osteosarcoma between 1996-2006, and controls were sampled from children and adolescents diagnosed with either nervous system tumors or leukemia during the same time frame, at a 4:1 control/case ratio. Using geocoded patient addresses at time of diagnosis, we estimated each patient's fluoride exposure level based on the fluoride level of their residence's public water supply (PWS). Unconditional logistic regression models were used to assess the association between osteosarcoma and fluoride level in drinking water, adjusting for several demographic risk factors. A total of 308 osteosarcoma cases, 598 leukemia controls, and 604 brain cancer controls met selection criteria and were able to be assigned a corresponding PWS fluoride level. Fluoride level was not associated with osteosarcoma, either when analyzed in a univariable analysis or when adjusting for age, sex, race, and poverty index. We also conducted stratified analyses by sex, and no association between PWS fluoride level and osteosarcoma was observed among either males or females. Our study found no relationship between the fluoride level in drinking water and childhood/adolescent osteosarcoma in Texas. Results should help to alleviate concerns about this issue in Texas.

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COMPARISON OF EXPOSURE ESTIMATION METHODS FOR AIR POLLUTANTS: AMBIENT MONITORING DATA AND REGIONAL AIR QUALITY SIMULATION. *Mercedes Bravo, Montserrat Fuentes, Yang Zhang, Michael Burr, Michelle Bell (Yale University, New Haven CT 06511)

Ambient monitors are often used to estimate air pollution exposure in epidemiological studies. This approach is efficient but has limitations, including restricted coverage and resolution. Air quality modeling has potential to address some limitations of monitoring networks. We evaluated application of a regional air quality model to estimate air pollution exposure for epidemiological studies. Individual and spatially-aggregated exposure estimates for $PM_{2.5}$ and O_3 were calculated for the eastern U.S. in 2002 using results from the Community Multiscale Air Quality (CMAQ) modeling system and an approach based on ambient monitoring data. Differences in populations included in monitor- versus model-derived exposure estimates were evaluated, and advantages and limitations of exposure estimation approaches were assessed. Exposure estimates generated from CMAQ provided greater spatial coverage and higher spatial and temporal resolutions compared to estimates from monitor data. The monitoring approach produced estimates for 370 counties for $PM_{2.5}$ and 454 for O_3. Modeled estimates included 1861 counties, covering 50% more population. Counties with monitors tended to be more urban, with a higher percentage of black residents, college graduates, young children, and higher median income and modeled pollutant levels. CMAQ slightly overestimated O_3 (annual normalized mean bias [NMB] = 4.30%); modeled $PM_{2.5}$ estimates were underestimated (NMB = -2.09%), with bias varying seasonally. Epidemiology may benefit from use of air quality models, with improved spatial and temporal resolutions and ability to study populations far from monitors that may differ from those near monitors. Model performance varied by pollutant, time of year, measure of performance, and exposure metric. Appropriateness of using modeled pollutant exposures in health studies depends on the pollutant, acceptable level of uncertainty, population of interest, study design, and other factors.

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OSTEOSARCOMA AND LOW-LEVEL RADIUM EXPOSURE IN DRINKING WATER - A CASE CONTROL ANALYSIS. *Jessie Gleason, Perry Cohn, Stasia Burger, Jerald Fagliano (New Jersey Department of Health, Trenton NJ 08625)

Findings from studies investigating radium in drinking water and the incidence of osteosarcoma have been mixed. We used a case-control design in which each cancer registry case of osteosarcoma 10 years of age or older diagnosed from 1996 to 2009 was frequency-matched by year of diagnosis, age at diagnosis, and sex to four controls. We selected two control groups. First selection includes individuals with any diagnosis of cancer excluding both leukemia and any bone cancers. The second referent selection includes individuals diagnosed with brain and central nervous system cancers. Cases and controls were geocoded - using residence at diagnosis - to community water systems in New Jersey for which the quality of radium characterization was considered sufficient. Cases and controls were assigned values of gross alpha radioactivity and potency-weighted combined radium-226 and radium-228 of the water system to which they were geocoded. Unconditional logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (95% CI) comparing exposed to unexposed. Exposure was defined as a gross alpha radioactivity or combined radium value greater than the maximum contaminant level. No association was found using either the first control group (OR = 1.01, 95% CI 0.35-2.89) or the second control group (OR = 1.10, 95% CI 0.34-3.58). The case-control design and use of strong environmental data strengthens our understanding of the risk of osteosarcoma from radium in drinking water.

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PRECONCEPTION AIR POLLUTION EXPOSURES INCREASE THE RISK OF GESTATIONAL DIABETES MELLITUS. *Candace Robledo, Pauline Mendola, Edwina Yeung, Rajeshwari Sundaram, Danping Liu, Qi Ying, Seth Sherman, Leah Lipsky, Laughon Katherine (National Institute of Child Health and Human Development, Division of Epidemiology, Statistics & Prevention Research, Rockville MD 20892)

Air pollutants such as particulate matter (PM) and nitrogen dioxide (NO2) have been linked to the development of type 2 diabetes, but no studies have examined their impact on the risk of gestational diabetes mellitus (GDM). Singleton pregnancies without pregestational diabetes (n = 220,264) from the Consortium on Safe Labor (2002-2008) were linked to pollutant exposures estimated using the Community Multi-scale Air Quality model. Average exposure within the 3-month window prior to pregnancy, defined as 91 days before the last menstrual period, was calculated for PM2.5, PM10, NO2, carbon monoxide (CO), sulfur dioxide (SO2) and ozone (O3). GDM diagnosis (n = 11,347) was ascertained from electronic medical records supplemented by discharge ICD-9 codes. Binary regression models with the log link function were fitted to estimate relative risks (RR) of GDM per 1-unit increase in pollutant concentrations adjusting for study site, maternal age and race. During the 3 months prior to pregnancy, criteria air pollutants, with the exception of ozone, increased the risk for GDM: PM2.5 (RR = 1.03, 95% CI: 1.02, 1.04), PM 10 (RR = 1.03, 95% CI: 1.02, 1.04), NO2 (RR = 1.03, 95% CI: 1.02, 1.04), SO2 (RR = 1.09, 95% CI: 1.07, 1.12), CO (RR = 1.0014, 95% CI: 1.0009, 1.0019) and O3 (RR = 0.99, 95% CI: 0.99, 1.00). In conclusion, we observed increased risk for GDM with air pollutants previously shown to be associated with type 2 diabetes (PM and NO2) and with other criteria air pollutants. Preconception may be a key exposure window with respect to the association between air quality and glucose intolerance during pregnancy.

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THE EFFECT OF URINARY BISPHENOL A ON SHORT-TERM REPEATED MEASUREMENTS OF ANDROGEN HORMONES AND INSULIN RESISTANCE: EWHA BIRTH & GROWTH COHORT STUDY.

*Hye Ah Lee, Young Ju Kim, Hwayoung Lee, Hye Sun Gwak, Eun Ae Park, Su jin Cho, Eun Hee Ha, Hae Soon Kim, Hyesook Park (Ewha Womans University, School of Medicine, Seoul, Republic of Korea)

Objectives: Using BPA exposure data of aged 7 to 8 girls without menarche from Ewha Birth & Growth Cohort, we investigated the effect of BPA on change of androgenic hormones [testosterone, androstenedione, and dehydroepiandrosterone (DHEA)] and insulin resistance during the one year follow up period. Methods: During July to August 2011, we conducted a follow-up examination of children aged 7 to 8 and then again one year later. Eighty of the 155 subjects (51.6%) were girls and 48 girls of them (60.0%) were examined twice. In the present study, urinary BPA measured once and categorized into tertiles. We repeatedly measured androgenic hormones, insulin, and glucose. To assess the effect of urinary BPA concentration on change of androgenic hormones and metabolic indices, we used multivariate analysis of variance (MANOVA) for repeated measures adjusting for potential confounders at baseline. Results: The median concentration of urinary BPA of subjects was 14.07ng/mL (inter-quartile range: 4.03-20.72ng/mL). In baseline, there was no significant difference between tertiles except for glucose. After one year later, those who in the top tertile showed higher level on androstenedeione and estradiol compared with the lowest tertile (Bonferroni corrected p value <0.05). In MANOVA, the significant main effect for group was observed in average of androstenedione, insulin, glucose, and homeostatsis model assessment (HOMA) index, and showed marginal signifcance levels in DHEA and testosterone. Moreover, girls in the top tertile had increased level of androstenedione [difference (d) = 1.04] while other groups showed decreased (d for intermediate tertile = -0.02, d for the lowest tertile = -0.28, respectively), but it was not statistically significant. Conclusions: This study suggests that further investigation is required to elucidate the mechanisms linking BPA with regulation for androgenic hormone. *This work was supported by National Research Foundation of Korea Grant funded by the Korean Government (2010-0026225).

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VARIATION IN OBSERVED EPIDEMIOLOGIC ASSOCIATIONS DUE TO CHOICE OF EXPOSURE METRIC.

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The use of human biomonitoring to characterize exposure to environmental contaminants has expanded greatly in recent years. However, substantial variability in effect measures may arise when using different exposure metrics—an example is the variability in reported associations between phthalates, and body mass index (BMI) and waist circumference (WC). The goal of this study is to evaluate the variability and potential bias in epidemiologic associations resulting from use of different exposure metrics in the 2005-2010 NHANES data. Metabolites of common phthalates (MBzP, MBP, MiBP, cx-MiNP, MEP, MEHP, MEHHP, MEOHP, and MECPP) were evaluated using the following exposure metrics: unadjusted urine concentration (either alone or including creatinine as a covariate), creatinine-adjusted urine concentration, and daily intake estimated using the creatinine-correction method. Linear regression models were constructed to examine the association between BMI or WC (after natural log transformation) and each phthalate exposure metric. Phthalate exposure metrics were included in two ways—either as continuous variables after natural log transformation, or as categorical variables based on quartiles of the distribution in the study population. All models were adjusted for age, sex, race/ethnicity and poverty index ratio. The pattern of phthalate levels by BMI varied across phthalates, and in multivariate regression each was associated with increased BMI and WC. For any given phthalate, the patterns of association with BMI or WC were generally similar when using exposure metrics of unadjusted urine concentration or estimated daily intake, while effect measures incorporating urinary creatinine were generally weaker. A simulation study is being performed to determine relative bias resulting from the use of each metric when the true association is known. Disclaimer: The views expressed in this manuscript are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.

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INDIVIDUAL AND NEIGHBORHOOD SOCIOECONOMIC STATUS, LONG TERM EXPOSURE TO AIR POLLUTION AND RISK OF CARDIOVASCULAR DISEASE.

*Gloria C Chi, Anjum Hajat, Chloe E Bird, Mark R Cullen, Beth Ann Griffin, Kristin A Miller, Regina A Shih, Marcia L Stefanick, Sverre Vedal, Eric A Whitsel, Joel D Kaufman (University of Washington, Seattle WA 98195)

Low socioeconomic status (SES) may increase susceptibility to air pollution due to increased exposure to pollutants and reduced resources to cope with adverse health outcomes. We examined whether low individual SES (ISES) or low neighborhood SES (NSES) confounded or modified the association between fine particulate matter exposure ($PM_{2.5}$, particles <2.5 μm in aerodynamic diameter) and incident cardiovascular disease (CVD) events in participants from the Women's Health Initiative Observational Study. Women with prior CVD, invalid $PM_{2.5}$ estimates, and missing data in any covariates were excluded (n = 48,067). $PM_{2.5}$ exposure at participants' residential address was predicted from a regionalized national universal kriging model using partial least squares regression. Hazard ratios (HR) for each 10 μg/m^3 increase in $PM_{2.5}$ exposure were estimated using Cox-proportional hazards models adjusting for age, race, and CVD risk factors. ISES and NSES were modeled as interactions with $PM_{2.5}$ or adjusted for as covariates. There were 2,446 CVD events and 536 CVD deaths over 11 years of follow-up. In fully adjusted models, $PM_{2.5}$ exposure was positively associated with CVD events (HR = 1.22; 95% confidence interval [CI]: 1.06, 1.40) and CVD deaths (HR = 1.31; 95% CI: 0.95, 1.81). This relationship was stronger among residents of disadvantaged neighborhoods. Women living in the lowest SES neighborhoods had an HR of 1.73 (95% CI: 1.33, 2.25) while those in the highest SES neighborhoods had HR 0.91 (95% CI: 0.63, 1.19). ISES did not modify the associations between PM and CVD outcomes, nor were ISES nor NSES strong confounders. Air pollution appears to disproportionately affect cardiovascular health of women who live in low SES neighborhoods and these women tend to experience greater $PM_{2.5}$ exposure as well.

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2000-2010 TRENDS IN HIV TESTING AMONG ADULTS AGED 18-44: A DECADE OF DISPARITIES.

*Jennifer Peregoy, Renee Gindi, Jacqueline Lucas (National Center for Health Statistics (CDC), Hyattsville MD 20782)

Rates of HIV testing grew rapidly early in the AIDS epidemic, with recent indications that the increase has slowed. This study uses the Healthy People 2020 (HP 2020) target of 16.9% tested in the past 12 months to evaluate recent trends in HIV testing among U.S. adults aged 18-44, by demographic and access to care characteristics. Data from the 2000-2010 National Health Interview Survey, conducted by the National Center for Health Statistics, were analyzed (n = 153,223 adults aged 18-44). Trends over the 11-year span were evaluated using orthogonal polynomials, and average annual percent change (AAPC) was calculated. From 2000 to 2010, the proportion of adults aged 18-44 who were tested for HIV in the past 12 months increased linearly from 13.1% to 13.7% (p-trend = 0.0006; AAPC = 0.9). Some subgroups have already met or exceeded the HP 2020 target, such as women, non-Hispanic black adults, and Hispanic adults. However, given the 2010 HIV testing levels and subgroup-specific AAPC observed from 2000-2010, several subgroups are not on track to reach the target by 2020. These subgroups include adults who are male (2010 estimate = 9.9%; AAPC = 0.0), non-Hispanic white (10.6%; -0.2), Asian (9.4%; -2.3), uninsured (13.1%; 0.5) or with private health insurance coverage (11.5%; 0.4), or deemed at lower risk for HIV infection (13.1%; 0.9). Monitoring trends in HIV testing permits identification of groups where testing rates persistently remain low. Additional public health efforts that increase the AAPC may be needed if all groups are to achieve the HP 2020 target for HIV testing.

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SEASONAL VARIATION IN BACTERIAL VAGINOSIS. *Mark Klebanoff (The Ohio State University, Columbus OH 43205)

Bacterial vaginosis (BV), a common disturbance of the vaginal microbial ecology, has been associated with adverse health outcomes including preterm birth and HIV acquisition. Vitamin D insufficiency has been associated with increased prevalence of BV in cross-sectional studies. If this association were causal a woman should be less likely to have BV in summer than in winter, due to higher serum vitamin D concentration in summer. Therefore the authors conducted a longitudinal, case-crossover study within the Longitudinal Study of Vaginal Flora cohort in Birmingham AL (33.5 degrees N) to compare a woman's BV (Nugent score ≥7) status in all 4 seasons of the year. The cohort enrolled 3620 non-pregnant women who underwent interview and exam every 3 months for a year; this analysis included women with at least 4 visits (2337 women, 11118 visits). BV prevalence in spring, summer and fall was compared to winter by conditional logistic regression. BV prevalence was 40.2% in winter (Dec-Feb), 38.2% in spring (Mar-May), 41.1% in summer (Jun-Aug) and 40.8% in fall (Sep-Nov). 1329 women changed BV status and were included in the conditional model. Matched odds ratios (95% CI) compared to winter were 0.93 (0.80-1.08) for spring, 1.18 (1.02-1.36) for summer and 1.11 (0.96,1.29) for fall; likelihood ratio p-value for season was 0.006. No effect measure modification was observed by race ($p = 0.56$). Adjustment for factors previously associated with BV that might vary with season (douching, number of recent sex partners, vaginal intercourse frequency, new sex partner in past 3 months, contraception type, smoking) changed the odds ratios and confidence limits by 0.01 or less. Although vitamin D status was not measured, these results do not support an association between vitamin D insufficiency and BV.

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PREDICTORS OF RETENTION IN A COHORT OF HIV/AIDS PATIENTS STARTED ON ANTIRETROVIRAL THERAPY IN ADDIS ABABA, ETHIOPIA. *David Sando (Management and Development for Health, Dar es Salaam Tanzania)

Background: Provision of free public antiretroviral therapy (ART) in Ethiopia begun in 2003, and since then much effort has been focused on increasing the number of those receiving the treatment. Black Lion Hospital was the first facility in the country to start providing HIV services, and by the end of March 2009 a total of 8914 People Living with HIV (PLHIV) were enrolled in the clinic, of which 6428 (72%) had been initiated on ART. In order to ensure the long-term success of the ART program it is critical that patients are retained in treatment and care. However, little is known about the predictors of retention among ART patients. Methods: We analyzed routine data collected from the cohort of patients aged 18 years or older receiving ART at Black Lion hospital who had initiated ART between June 2006 and June 2009. We estimated retention rates and predictors of non-retention in survival analyses. Results: Among the 551 patients enrolled in the study, 117 (21%) were lost to follow up and 68 (12%) were reported dead. The patient's median follow up period was 10 months (IQR 3-18) after the start of ART. The estimated probabilities of retention were 85%, 80%, 71%, and 51.5% at 3, 6, 12 and 24 months respectively. Retention was found to be significantly high among those who started ART with normal HB as compared to those with moderate anemia (adjusted Hazard Ratio (aHR= 0.597, CI: 0.429-0.869; $P = 0.0062$) or severe anemia (aHR = 0.439, CI: 0.322-0.638; $P < 0.0001$) . The study also found out that patients presenting with advanced HIV disease (WHO clinical stage IV) are less likely to be retained in treatment clinic (aHR = 1.410, CI: 1.037-1.863; $P = 0.0274$). Conclusion: We found remarkable poor retention of patients in this cohort of ART patients in Ethiopia. To improve retention, it will be critical to ensure that patients initiate ART before the suffer severe HIV disease and to ensure good general health recovery.

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THE EFFECT OF BOOSTED LOPINAVIR VERSUS BOOSTED ATAZANAVIR-CONTAINING REGIMENS ON IMMUNOLOGIC, VIROLOGIC AND CLINICAL OUTCOMES IN A PROSPECTIVE OBSERVATIONAL STUDY. Lauren E Cain on behalf of the HIV-CAUSAL Collaboration (Department of Epidemiology, Harvard School of Public Health, Boston MA 02115)

We used observational data from the HIV-CAUSAL Collaboration to compare first-line regimens consisting of either ritonavir-boosted lopinavir or ritonavir-boosted atazanavir and two or more nucleoside reverse transcriptase inhibitors (NRTIs). HIV-infected, antiretroviral-naive, and AIDS-free individuals were followed from the time they started an NRTI, ritonavir, lopinavir or atazanavir, classified as following one or both types of regimens at baseline, and censored when they started an ineligible drug or at 6 months if their regimen was not yet complete. We estimate the "intention-to-treat" effect for atazanavir versus lopinavir regimens on clinical, immunologic, and virologic outcomes. Our models included baseline covariates and adjusted for potential bias introduced by censoring via inverse probability weighting. A total of 8,694 individuals initiated a lopinavir regimen (158 deaths, 434 AIDS-defining illnesses) and 4,999 individuals initiated an atazanavir regimen (44 deaths, 137 AIDS-defining illnesses). The adjusted intention-to-treat hazard ratios (95% confidence interval) for atazanavir versus lopinavir regimens were 0.81 (0.54, 1.23) for death, 0.93 (0.75, 1.15) for AIDS-defining illnesses or death and 0.82 (0.68, 1.00) for virologic failure (HIV-RNA > 50 copies/ml) at 12 months. The 12-month increase in CD4 cell count was almost identical in both groups. We found little evidence of differences between the atazanavir and lopinavir regimens with respect to mortality, incidence of AIDS-defining illnesses, 12-month increase in CD4 cell count, and risk of virologic failure at 12 months. As for all observational studies, the validity of our results rests on the assumption that the measured covariates were sufficient to adjust for confounding.

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THE ROLE OF ALCOHOL/DRUG ABUSE AND TREATMENT IN APPOINTMENT ATTENDANCE AND VIROLOGIC RESPONSE AMONG HIV+ AFRICAN AMERICANS. *Chanelle Howe, Michael Mugavero, Stephen Cole, Sonia Napravnik, Jay Kaufman, Adaora Adimora, Joseph Eron (Department of Epidemiology, Center for Population Health and Clinical Epidemiology, Brown University Program in Public Health, Providence RI 02912)

Prior work showed that among HIV+ patients, missed clinic appointments partially explained why virologic failure (i.e., detectable plasma HIV RNA while on therapy) was more common among African Americans (AA) than Caucasians (Mugavero et al. JAIDS 2009,50:100-8). We estimated the effect of alcohol/drug abuse and treatment on attending scheduled appointments and virologic success among 539 AA patients with scheduled HIV primary care appointments in the UAB 1917 Clinic Cohort between 1/1/2007 and 8/1/2011 using modified Poisson regression models. Models were adjusted for age, first visit date, gender, an AIDS diagnosis, CD4 count, time on antiretroviral therapy, time since last attendance or success, appointment or RNA assessment number, education, insurance, as well as prison, long-term drug/alcohol abuse, and mental illness history. At the first clinic visit, the median (quartiles) age and CD4 count was 36 (28; 44) years and 337 (145; 543) cells/mm^3, respectively. During follow up, 32% of patients had abused or received treatment for alcohol/drugs in the prior year while half had attended at least 80% of appointments and achieved virologic success for at least 60% of RNA assessments. Compared to patients who abused without treatment, the adjusted risk ratio (RR) for attending scheduled appointments was 1.07 (95% confidence limits: 0.73, 1.58) among patients who did not abuse and were not in treatment, 1.08 (0.71, 1.63) among patients who did not abuse while in treatment, and 0.64 (0.49, 0.85) among patients who abused while in treatment. The corresponding adjusted RRs for virologic success were 1.25 (0.62, 2.49), 1.11 (0.50, 2.47), and 1.18 (0.77, 1.80). Among HIV+ AA UAB patients, alcohol/drug treatment among concurrent abusers may decrease attendance yet increase the likelihood of virologic success. Abuse appeared to decrease attendance overall, but decrease virologic success only among those not in treatment. However, RR estimates were imprecise.

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ANTIRETROVIRAL PENETRATION INTO THE CENTRAL NERVOUS SYSTEM AND THE INCIDENCE OF AIDS-DEFINING NEUROLOGICAL CONDITIONS: A PROSPECTIVE OBSERVATIONAL STUDY. Ellen C. Caniglia on behalf of the HIV-CAUSAL Collaboration (Harvard University School of Public Health Department of Epidemiology, Boston MA 02138)

Objective: To compare regimens with different Central Nervous System Penetration Effectiveness (CPE) scores among HIV-infected, antiretroviral-naive, and AIDS-free individuals with respect to the incidence of four AIDS-defining neurological conditions (neuroAIDS): HIV dementia, toxoplasmosis (TOXO), cryptococcal meningitis (CM), and progressive multifocal leukoencephalopathy (PML). Design: Prospective studies of HIV-infected individuals in Europe and the US included in the HIV-CAUSAL Collaboration, 1998-2012. Methods: Antiretroviral therapy-naive individuals were followed from the time they started a complete antiretroviral regimen (cART). We classified regimens as having a low (<8), medium (8-9), or high (>9) CPE score at baseline (Letendre S. Background and Rationale of the CPE Score. In: *2nd International Workshop on HIV & Aging*. Baltimore, MD; 2011). We used inverse probability weighting to adjust for potential bias due to loss to follow-up. Using a pooled logistic regression model, we estimated intention-to-treat hazard ratios for regimens with high and medium CPE scores compared with regimens with a low score for each of the four neuroAIDS conditions. Results: 19,730 individuals (55%) initiated a regimen with a low CPE score, 11,870 (33%) with a medium CPE score, and 4,158 (12%) with a high CPE score. During follow-up, there were 105 cases of HIV dementia, 100 cases of TOXO, 69 cases of CM, and 79 cases of PML. Compared with a low CPE score, the hazard ratio (95% confidence interval (CI)) for a high CPE score was 1.95 (1.06, 3.61) for HIV dementia, 1.06 (0.53, 2.11) for TOXO, 0.95 (0.41, 2.18) for CM, and 1.33 (0.65, 2.73) for PML. Compared with a low CPE score, the respective hazard ratios (95% CIs) for a medium CPE score were 1.13 (0.68, 1.86), 0.89 (0.56, 1.42), 1.50 (0.87, 2.57) and 1.07 (0.63, 1.80).Conclusion: Initiation of a cART regimen with a high CPE score increases the risk of HIV dementia, but not of other neuroAIDS conditions.

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PRIMARY ANTIFUNGAL PROPHYLAXIS FOR CRYPTOCOCCAL MENINGITIS AND IMPACT ON ALL-CAUSE MORTALITY IN HIV-INFECTED PATIENTS:A SYSTEMATIC REVIEW AND META-ANALYSIS. *Richard Ssekitoleko, Moses Kamya, Arthur Reingold (University of Berkeley, Berkeley CA 94702)

Objective: To evaluate the role of primary antifungal prophylaxis for prevention of cryptococcal meningitis or all-cause mortality in HIV-infected patients. Design: Systematic review and meta-analysis of randomized trials and observational studies. Methods: PubMed, Google Scholar, Embase and Cochrane data bases were searched for studies evaluating if primary antifungal prophylaxis prevents cryptococcal meningitis or all-cause mortality. Quality assessed using different criteria depending on study type.Publication bias was assessed. Sub-group and sensitivity analyses were done. Due to homogeneity, results of meta-analysis for prevention of infection gave the fixed-effects model.The random effects model was used for results of all-cause mortality, due to heterogeneity. Findings: 13 studies assessed for prevention of infection,the summary risk ratio (RR) was 0.2(Fixed effects 95% CI: 0.13-0.30) $p < 0.0001$. 8 studies assessed for impact on all-cause mortality,the summary RR was 0.95(Random effects 95% CI: 0.76, 1.38) $p = 0.613$. On subgroup analysis for all-cause mortality, studies in resource limited settings gave a summary RR of 0.63 (Random effects shore adjusted 95% CI: 0.6, 1.53) $p = 0.84$. Most studies done in resource limited settings showed reduced cryptococcal meningitis-specific mortality. Conclusions: Primary antifungal prophylaxis prevents cryptococcal meningitis in advanced HIV-infection, but does not confer survival benefit overall. In resource limited settings this may lead to reduced mortality from cryptococcal meningitis and should be recommended irrespective of the cryptococcal antigen test results. Studies are needed to determine dose, frequency and duration of primary antifungal prophylaxis and timing of antiretroviral therapy for those on primary prophylaxis.

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THE INFLUENCE OF COLLEGE STUDENTS IN A SEXUAL NETWORK OF YOUNG AFRICAN-AMERICAN MEN. *Dana K Pasquale, Irene A Doherty, Michael E Emch, William C Miller, Evelyn Foust, Peter A Leone (UNC-Chapel Hill Gillings School of Global Public Health, Chapel Hill NC 27599)

Background: Young Black men who have sex with men (MSM) are disproportionately affected by HIV and STIs in North Carolina (NC). Behavior and STI prevalence in the sexual network affect transmission risk; network position may be a marker for risk. Methods: We constructed the local social and sexual network from reportable HIV and syphilis cases diagnosed among Black men age 15-30 in north central NC from 2006-2009 ($N = 1100$); infected and uninfected contacts were included in the network. Bonacich power is an unbounded measure of network centrality derived from the number of contacts and number of contacts' contacts. Higher Bonacich scores represent increased centrality in the network, while accounting for the centrality of an individual's contacts. It is iterative, giving more weight to closer contacts. To assess the centrality of college status in the network, Bonacich scores and 95% confidence intervals (95% CI) were calculated for all college-age Black men (17-24 years) ($n = 385$). We computed t-tests and chi-square tests to measure score differences by college status for factors associated with HIV infection risk. Results: Bonacich scores were normally distributed (range -57.5–62.2). Mean Bonacich score was higher for college than non-college men (5.86 (95% CI: 4.69-7.04) v. 3.13 (95% CI: 2.51-3.76), $P < 0.0001$). College men were more likely to use dating sites and less likely to use marijuana than non-college men. Sexual orientation also differed significantly by college status: while the proportion of MSM was ~70%, college men were more likely to be bisexual (24% v. 11%) and less likely to be heterosexual (7% v. 22%) compared to non-college men. College status was not associated with diagnosis, STI history, alcohol use, or having anonymous partners. Conclusion: Young African-American college men are more central in this sexual network than young African-American men who are not in college, putting them at risk for HIV acquisition and transmission.

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IMPACT OF HIV INFECTION ON HODGKIN LYMPHOMA CASES IN THE UNITED STATES. *Meredith Shiels, Erik Koritzinsky, Christina Clarke, Lindsay Morton, Eric Engels (National Cancer Institute, Rockville MD 20892)

Background: Hodgkin lymphoma (HL) occurs rarely in the U.S. However, HL risk is elevated 11-fold in people with HIV infection, and the number of HL cases in people with HIV has increased over time. Thus, despite the low HIV prevalence in the U.S, the HIV epidemic may have contributed substantially to the overall burden of HL. Methods: Ten U.S. cancer registries in the Surveillance, Epidemiology and End Results program recorded the HIV status of HLs from medical records during 1992-2009. Using these data, we estimated the proportion of HL cases with HIV by sex, age, calendar period and HL subtype. Results: 762 (4.4%) of 17,455 HL cases were HIV-infected at diagnosis. The proportion of HL cases with HIV was greater among males than females (7.1 vs. 1.0%). Among both males and females, the proportion of HL cases with HIV infection was greatest among 40-59 year-olds (13.6% and 1.8%, respectively), and among non-Hispanic blacks (17.3% and 2.9%) and Hispanics (12.0% and 1.9%). Among HL subtypes, the proportion of HIV-infected cases was greater for lymphocyte-depleted (males: 14.6%, females: 3.3%), mixed cellularity (males: 12.1%, females: 2.4%), and classical HL, not otherwise specified (males: 14.4%, females: 1.9%) than for lymphocyte-rich (males: 2.3%, females: 0%) and nodular sclerosis HLs (males: 3.8%, females: 0.7%). Conclusions: Due to a strong association with immunosuppression, a substantial proportion of HL cases in the U.S. are HIV-infected. These proportions are highest among men aged 40-59 years and among cases of lymphocyte-depleted and mixed cellularity HL. Our results highlight the importance of HIV testing among certain groups of HL patients.

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CONTRIBUTIONS TO CHANGING CANCER INCIDENCE IN THE U.S. HIV POPULATION, 1996-2008. *Hilary Robbins, Ruth M Pfeiffer, Meredith Shiels, Eric Engels (National Cancer Institute, Rockville MD 20852)

Introduction: HIV-infected (HIV+) people have elevated risk for some cancers, but rates have changed over time. Trends may reflect changes in 1) demographics of the HIV population, 2) general population (background) cancer rates, or 3) relative risks associated with HIV. We assessed the contributions of these factors to trends in 10 cancers during 1996-2008. Methods: Poisson models were applied to data from the U.S. HIV/AIDS Cancer Match Study to estimate annual percent changes (APCs). We evaluated the above contributions to HIV+ cancer trends by assessing trends 1) adjusted for demographics, 2) in background rates, and 3) in standardized incidence ratios (SIRs). Results: Cancer rates among HIV+ people rose for anal, colorectal, liver, and prostate cancer (APC 8.9%, 95% CI 4.7, 13.3), but declined for Hodgkin lymphoma (HL), cervical cancer, non-Hodgkin lymphoma (NHL), lung cancer (APC -2.9%, 95% CI -4.9, -0.8), and Kaposi sarcoma (KS, 1996-2001: APC-24.9%, 95% CI -27.8, -22.0). Breast cancer showed no trend. Adjustment for demographics attenuated and intensified trends in prostate and lung cancer, respectively (adjusted APCs 2.4% and -6.8%). Background rates changed over time for anal, lung, prostate, cervical, and liver cancer (APC 6.2%, 95% CI 4.3, 8.1). SIR trends were present for HL, lung cancer, cervical cancer, KS (1996-2001: APC -20.1%, 95% CI -25.2, -17.9), and NHL (1996-2003: APC -15.0%, 95% CI -16.7, -13.2). Conclusions: Demographic shifts in the HIV population contributed to increases in prostate cancer, but partly obscured declines in lung cancer. While background rates drove trends in some non-AIDS defining cancers (anal, lung, prostate, and liver cancer), falling relative risks largely explained declines in AIDS-defining cancers (KS, NHL, and cervical cancer).

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ANTIRETROVIRAL THERAPY ADHERENCE AND USE OF AN ELECTRONIC SHARED MEDICAL RECORD AMONG HIV-POSITIVE INDIVIDUALS. *Michael Silverberg, Wendy Leyden, Christine Stewart, James Ralston, Michael Horberg, Louis Grothaus, Sheryl Catz (Kaiser Permanente Northern California, Oakland CA 94610)

Background. Patient web sites with shared medical records (SMR) are an emerging healthcare technology allowing patients to communicate with providers, refill prescriptions, schedule appointments and view portions of their medical record including test results. Our objective was to determine whether SMR use was associated with antiretroviral therapy (ART) adherence for HIV+ individuals, which is key for successful outcomes in this population. Methods. We identified all HIV+ adults who used the SMR within two years of initial rollout in two large integrated healthcare systems. The primary outcome was change in ART refill adherence comparing the 12-month period before initial SMR use (baseline) with the 12-month period starting 6 months after a patient first used the SMR. Changes in adherence were also measured for age- and sex-matched nonusers before and after a randomly assigned reference date. Among users, we also evaluated whether frequency of SMR use (i.e. # of days during month using any SMR service), was associated with changes in adherence. Linear regression models adjusted for age, sex, health plan, race/ethnicity, baseline CD4 and HIV RNA. Results. We identified 1,638 HIV+ SMR users with 90% baseline adherence and 1,014 nonusers with 88% baseline adherence. Among users, high adherence was maintained over time (change: -0.11%; 95% CI: -0.83%, 0.62%). Among nonusers, mean adherence declined over time (change: -2.05%; 95% CI: -2.92, -1.18) ($P = 0.003$ comparing SMR users and nonusers). Among SMR users, high adherence was maintained only for those who used the SMR more frequently with changes of -1.62% (95% CI: -2.94, -0.31), -0.23% (95% CI: -1.50, 1.04), 0.41% (95% CI: -0.69, 1.50), and 0.97% (95% CI: -0.60, 2.54) for <0.5, <1, <2, and ≥2 SMR uses/month, respectively ($P = 0.007$ for comparison across categories). Conclusion. SMR use, particularly more frequent monthly use, is associated with maintaining high ART adherence over time among HIV+ patients.

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RELATIONSHIP OF CUMULATIVE IMMUNOLOGIC AND VIROLOGIC RESPONSE TO ANTIRETROVIRAL THERAPY (ART) WITH NON-AIDS-DEFINING CANCER (NADC) INCIDENCE, CFAR NETWORK OF INTEGRATED CLINICAL SYSTEMS. *Elizabeth Yanik, Sonia Napravnik, Stephen Cole, Chad Achenbach, Satish Gopal, Dirk Dittmer, Andrew Olshan, Mari Kitahata, Michael Mugavero, Michael Saag, Kenneth Mayer, Joseph Eron (University of North Carolina at Chapel Hill, Chapel Hill NC 27599)

Background: NADC burden is increasing in HIV populations, but factors associated with incidence remain unclear. We assessed associations between ART response and subsequent NADCs. Methods: We included patients with ≥1 CD4 count and HIV RNA measure post-ART start between 1996-2011 in CNICS, a clinical cohort. ART was defined as 3+ antiretrovirals. CD4 count-years and viremia copy-years were used as cumulative measures of virologic and immunologic ART response using multiple laboratory results. Patients were followed from 6 months post-ART to the first of: NADC, death, drop-out, 10 years post-ART, or last date of cancer ascertainment. Cox regression with inverse probability weights was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Results: Of the 9389 patients included, the median CD4 at ART start was 200 cells/mm^3 (IQR:60-332) and median HIV RNA was 4.8 log10copies/ml (IQR:4.3-5.4). Six months post-ART, the median CD4 was 304 cells/mm^3 (IQR:163-469) and 64% of patients had undetectable HIV RNA (<400 copies/mL). In total, 164 NADCs were diagnosed; 65 (40%) presumed virus-related. Most common NADCs were anal cancer ($N = 26$) and lung cancer ($N = 22$). In weighted analysis, CD4 count-years was associated with lower NADC incidence (HR per 200 cell*year/mm^3 increase: 0.98, 95% CI: 0.95-1.02). CD4 count-years was strongly associated with virus-related NADCs (HR per 200 cells*years/mm^3 increase: 0.92, 95% CI: 0.85-0.98), and unassociated with virus-unrelated NADCs. Viremia copy-years were not associated with virus-related or virus-unrelated NADC incidence. Conclusion: Poor immunologic response post-ART may increase NADC incidence by increasing risk of acquisition or persistence of oncogenic viruses. Poor immunologic status could also be a result of subclinical cancer. Virologic response was not independently associated with NADC incidence.

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HYPERTENSION AND HYPERGLYCEMIA IN A HAART NAïVE HIV POSITIVE POPULATION IN DAR ES SALAAM, TANZANIA. *Marina Njelekela, Akum Aveika, Alfa Muhihi, Donna Spiegelman, Claudia Hawkins, Catharina Armstrong, Enju Liu, James Okuma, Chalamila Guerino, Sylivia Kaaya, Ferdnand Mugusi, Wafaie Fawzi (Muhimbili National Hospital, Dar es Salaam Tanzania)

Background: Changes in blood pressure and blood glucose have been reported among treatment naïve HIV-infected patients in developed countries, however, data from developing countries are still scarce. Methods: Cross-sectional analysis of blood pressure and glucose was conducted among non-pregnant HAART-naïve patients enrolled from 2004-2008 in MDH-PEPFAR funded HIV Care and treatment program in Dar es Salaam, Tanzania. Hypertension was defined as SBP/DBP ≥140/90 mmHg; diabetes mellitus (DM) as random blood glucose (RBG) ≥200mg/dl, and hyperglycemia as RBG ≥140mg/dl. Relative risks (RR) were estimated using log-binomial regression models to examine the predictors of hypertension, diabetes and hyperglycemia. Results: Prevalence of hypertension was 12.5%, hyperglycemia 3.1% and DM 1.2%. Hypertension was 11% higher among men (RR = 1.11, 95% CI 1.05-1.18) and two-fold higher (RR = 2.30, 95% CI 2.14-2.49) among patients aged 50 years and above compared to patients aged 30-39 years ($p < 0.001$). After adjusting for age, sex, BMI, CD4 and WHO stage, hypertension was 36% lower in patients with CD4 <50cells/mm^3 compared to those with ≥200cells/mm^3 ($p < 0.001$). Likewise, hypertension was 40% lower among patients with WHO clinical stage IV disease ($p < 0.0001$) and 15% lower among those with history of TB treatment ($p < 0.01$). Prevalence of DM was 53% higher among men (RR = 1.53, 95% CI 1.10-2.12) and 63% higher (RR = 1.63, 95% CI 1.00-2.67) among patients age 50 years and above compared to patients aged 30-39 years. Conclusions: Immune dysfunction was associated with lower systolic and diastolic BP, with no variability in random blood glucose levels. BMI, male gender and age were important predictors of both high blood pressure and elevated random blood glucose. HIV treatment programs should screen and manage these risk factors even prior to HAART initiation and carefully monitoring patients for complications of HIV and its treatments. Keywords: Hypertension, Hyperglycemia, Diabetes Mellitus, HIV-positive, HAART naïve, Tanzania

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THE ASSOCIATION BETWEEN THE MEDICAL HOME AND PEDIATRIC DEVELOPMENTAL SCREENING AMONG US CHILDREN 5 YEARS AND YOUNGER. *Nicole Richmond, Tri Tran, Susan Berry (Louisiana State University Health Sciences Center, School of Medicine, New Orleans LA 70112)

The medical home is associated with increased acquisition of key healthcare services. Notably, a medical home policy is to provide pediatric developmental screening for developmental delay at ages 9, 18, and 30 months old. This longitudinal evaluation method helps to assess the duration, intensity, and/or accumulation of child and family risk factors that may have a temporal influence toward imparting phenotypic aberrations in normal development. In this study we assessed the association between the medical home and pediatric developmental screening among US children 5 years and younger, using data from 2007 national survey of children's health. Multilevel logistic models were applied. Clusters are states, and the pediatric developmental screening probability was modeled as a function of the medical home adjusted for tested confounders. Confounding variables are: age, insurance, race, special health care need, family structure, and census bureau region. Population weighted 81% (22,270) of US children 5 years and younger met study inclusion criteria (valid responses for study variables). Of this group 19.5% (4,310) received a pediatric developmental screening, and 63% (14,415) have a medical home. The 51state adjusted models indicate much variation with odds ratios (OR) and 95% confidence intervals (95% CI) ranging from an inverse to increased association. The random intercept and slope model has the best fit: medical home increased the pediatric developmental screening odds by 24% (OR: 1.24, CI 95%: 1.10, 1.38). Our findings show the medical home - pediatric developmental screening association is partially influenced by an individual's state. This work portends a need to preliminary assess for state variation when analyzing individual health outcomes. Early examination may indicate that national policy has a differential impact across states perhaps due to disparate state policy. Despite notable state differences we found a supportive role of the medical home with higher pediatric developmental screening rates.

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CHILDHOOD GROWTH TRAJECTORIES BY COMBINATIONS OF MATERNAL WEIGHT STATUS BEFORE PREGNANCY AND MATERNAL SMOKING DURING PREGNANCY: A MULTILEVEL ANALYSIS. *Kohta SUZUKI, Miri SATO, Zentaro YAMAGATA (University of Yamanashi, Chuo Yamanashi Japan)

Maternal weight status before pregnancy and maternal smoking during pregnancy are significantly associated with fetal and childhood growth. However, few studies have examined the association between childhood growth and combinations of both factors using multilevel analysis. This study aimed to describe the difference in childhood growth trajectories by these combinations, using data from a prospective cohort study in Japan. The study participants were 1973 women and their singletons who were born between April 1, 1991, and March 31, 2003. Children were categorized as born from normal-weight and non-smoking mothers (NN), normal-weight and smoking mothers (NS), underweight and non-smoking mothers (UN), underweight and smoking mothers (US), overweight and non-smoking mothers (ON), and overweight and smoking mothers (OS). Birth weight and anthropometric data were collected from 1965 (at birth, 99.6%), 1655 (at age 3, 83.9%), 1527 (at age 5, 77.4%), 1497 (at age 7–8, 75.9%), and 1501 (at age 9–10, 76.1%) of these children. Multilevel analysis including both individual and age as different level variables by gender of children was used to describe the trajectories of body mass index (BMI) z-scores for statistical analyses. Although children of the OS group were the leanest at birth, their BMI increased rapidly by 3 years of age. Moreover, male children of the NS and ON groups were also likely to increase their BMI. On the other hand, a different trend was observed among female children. Only female children of the US group were likely to decrease their BMI from 5 years of age. In addition, there was no remarkable difference in BMI trajectories among children of the other groups. In conclusion, childhood growth trajectories differed by combinations of maternal weight status before pregnancy and maternal smoking during pregnancy. Further, a gender difference existed in the association between childhood growth and the combinations.

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PREVENTIVE DENTAL SEALANTS AND BEHAVIORAL, NEUROPSYCHOLOGICAL, OR PHYSICAL DEVELOPMENT IN CHILDREN. *Nancy Maserejian, Peter Schrader, Mary Tavares, Jennifer Soncini, Russ Hauser, David Bellinger, Felicia Trachtenberg (New England Research Institutes, Inc., Watertown MA 02472)

Resin-based dental composite materials release their components during placement and over time as materials degrade, but the health effects of the resin monomers are unknown. We previously analyzed associations between composite fillings and health outcomes in the New England Children's Amalgam Trial (1999-2005) study cohort (N = 534), finding that composites were associated with worse psychosocial, but not neuropsychological or physical, outcomes. All trial participants (baseline age 6-10 y) were also offered preventive sealants, which contain similar resins as the composite fillings. The aim of the current analysis was to test the hypothesis that sealants are associated with these health outcomes over the 5-year follow-up. Multivariable generalized linear models were used to test associations between surface-years (SY) of sealants and behavioral or neuropsychological test score changes, adjusting for sociodemographic confounders and composite fillings. Physical growth changes were analyzed with repeated measures models; survival analysis was used for the outcome of menarche among a subset of girls (n = 113). Mean (SD) sealant exposure level at end of follow-up was 39.1 (20.9) SY. Sealants were not associated with behavior assessment scores (e.g. total problems: Behavior Assessment for Children, 10-SY Beta = -0.4, SE = 0.2, P = 0.06; Child Behavior Checklist 10-SY B = -0.2, SE = 0.3, P = 0.6) or neuropsychological tests (e.g. full-scale IQ, 10-SY B = 0.1, SE = 0.2, P = 0.6). No associations were found for body mass index changes (B = -0.02 SE = 0.02, P = 0.4), body fat % (girls B = -0.2 SE = 0.3; boys B = -0.1 SE = 0.3), or menarche (hazard ratio = 0.99, 95% CI 0.98-1.00, P = 0.15). Except for menarche, most beta estimates for sealants were in the opposite direction of estimates for composite. This analysis showed no significant associations between preventive dental sealants and behavioral, neuropsychological, or physical development in children over the 5-year follow-up.

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LIFE COURSE ADIPOSITY AND ADOLESCENT DEPRESSIVE SYMPTOMS: EVIDENCE FROM HONG KONG'S "CHILDREN OF 1997" BIRTH COHORT. *Hui Wang, Tai Hing Lam, Gabriel M Leung, Catherine Mary Schooling (The University of Hong Kong, Hong Kong SAR China)

Depression often emerges in adolescence, and is a major public health issue. Adiposity may be a factor in the emergence of depression. However, in western settings both adiposity and depression tend to be socially patterned, making it unclear whether the observed association is biologically based or contextually specific. The authors used multivariable partial least squares regression to assess the association of birth weight and life course adiposity with adolescent depressive symptoms score at ~14 years, assessed from Patient Health Questionnaire(PHQ-9), in a non-western context with little social patterning of adiposity using the Chinese "Children of 1997" birth cohort in Hong Kong. PHQ-9 was available for 5797 term births (73% follow-up by August 2012). A total of 259 adolescents (4.5%) had PHQ-9 score of 11 or more potentially corresponding to depression. Average PHQ-9 scores were 3.4 in girls and 2.9 in boys. Using PHQ-9 as a continuous depressive symptom score, birth weight z-score, BMI z-scores at 3 months, 9 months, 3 years, 7 years, 9 years, 11 years, 12 years and successive BMI z-scores changes had little association with PHQ-9 at 14 years, adjusted for socio-economic position, parental depressive symptoms and survey mode. Life course adiposity does not appear to be a factor in the development of depressive symptoms in adolescence.

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ASSOCIATION BETWEEN SLEEP-WAKE PATTERNS AT 3 YEARS OF AGE AND OVERWEIGHT STATUS AT 9–10 YEARS OF AGE IN JAPAN. *Ayasa Takahashi, Kohta Suzuki, Miri Sato, Sonoko Mizorogi, Zentaro Yamagata (University of Yamanashi, Chuo Yamanashi Japan)

Although recent epidemiological studies have suggested that short sleep duration is associated with childhood obesity, the mechanisms of this association are not clear. Hormonal effects are thought to be responsible for this association. Thus, not only sleep duration but also the time of sleep onset and waking, which might be associated with hormone secretion, should be studied. This study aimed to examine the association between sleep-wake patterns at 3 years of age and overweight status at 9–10 years of age. The study population comprised 2524 children born in Japan between 1991 and 2003, who were not obese at 3 years of age. Anthropometric data was obtained from 2214 of these children at the age of 9–10 years (follow-up rate, 87.1%). Of these participants, 254 (11.4%) were classified as overweight at 9–10 years of age. We found no significant association between sleep duration at 3 years of age and overweight status at 9–10 years of age. We then classified the children according to their sleep-wake patterns at the age of 3 years into 4 groups by considering the time of sleep onset (before 22:00 vs. at/after 22:00) and waking (before 08:00 vs. at/after 08:00). The early sleep-early wake pattern (EE), early sleep-late wake pattern, late sleep-early wake pattern (LE), and late sleep-late wake pattern (LL) was seen in 831 (37.5%), 21 (0.9%), 1044 (47.2%), and 198 (8.9%) participants, respectively. After adjusting for gender, sleep duration, kindergarten enrollment, and body mass index at 3 years of age, LE and LL children were more likely to be overweight at 9–10 years of age than EE children (odds ratio [OR] 1.4, 95% confidence interval [CI] 1.0–2.0 and OR 1.9, 95% CI 1.2–3.0, respectively). In conclusion, the sleep-wake pattern at the age of 3 years is a determinant for overweight status at 9–10 years. These findings suggest that sleep-wake patterns should be considered when examining the association between sleep duration and childhood obesity.

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DIFFERENCE IN PUBERTAL HEIGHT GAIN TRAJECTORIES BASED ON GENDER AND CHILDHOOD BODY MASS INDEX: A MULTILEVEL ANALYSIS. *Wei Zheng, Kohta Suzuki, Miri Sato, Zentaro Yamagata (University of Yamanashi, Chuo Yamanashi Japan)

Recently, a trend towards earlier pubertal growth has been identified along with an increase in childhood obesity rates. Therefore, it is important to determine the current growth pattern and elucidate the factors influencing it. However, longitudinal studies using multilevel analysis are limited. Hence, this study aimed to evaluate pubertal height gain trajectories in Japanese school-aged children first by gender and then by gender-based childhood body mass index (BMI). This study included 2450 children born between 1991 and 2003 in Japan. These children were followed up from first-grade at elementary school (age range, 6-7 years) to third-grade at a junior high school (age range, 14-15 years) and their anthropometric data were collected annually. Annual height gain trajectories were constructed by multilevel analysis because repeated measurements were used. Of the participants, 12.2% (153/1281) of boys and 11.9% (143/1169) of girls were classified as overweight/obese based on their BMI at baseline. Gender-based height gain trajectories showed that in girls, annual height gain increased slowly and peaked between ages 9.5 and 11.5 years, while in boys, the height gain declined slightly at first and peaked between ages 11.5 and 12.5 years. The gender-based difference in height gain was significant between ages 7.5 and 14.5 years ($p < 0.0001$). In both genders, obese/overweight children exhibited a greater increase in height until the peak age of height gain, after which a decline in height gain was observed at an earlier age. Peak height gain was observed in obese/overweight girls at an earlier age compared to their non-overweight peers. In conclusion, although differences in gender-based height gain trajectories were significant, a trend that obese/overweight children grew faster in the early pubertal stages, while their non-overweight peers attained similar growth at a later age, was observed in both genders.

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INFLUENZA VACCINATIONS FOR CHILDREN LIMITED BY UNMET HEALTHCARE NEED WITHIN THEIR FAMILIES. *Lauren Wisk, Whitney Witt (Department of Population Health Sciences, University of Wisconsin, Madison, Madison WI 53726)

The importance of childhood preventive care, including vaccinations, is well known; however, less than half of all children and adolescents in the US receive the preventive care recommended by professional guidelines. We sought to determine if unmet healthcare need was associated with receipt of influenza vaccinations among children and adolescents in the US, using a nationally representative, population-based sample. We examined data on 61,544 children from the 2005-2010 National Health Interview Survey. Unmet healthcare need was defined as delayed or forgone healthcare during the past 12 months due to cost, for the child and for any other family member. Child's receipt of flu shot or spray was examined during the 12 months prior to the survey. Overall, 28.6% of children received a flu vaccine, and 4.9% of children experienced unmet healthcare need while an additional 15.5% had a family member who experienced unmet healthcare need. Multivariate regression results indicated that children who directly experienced unmet healthcare need did not have lower odds of vaccine receipt (OR: 0.94, 95% CI: 0.82-1.08) but children who had a family member that experienced unmet need had 12% lower odds of vaccine receipt (OR: 0.88, 95% CI: 0.83-0.94) compared to children in families with no unmet need. Additional disparities in vaccine receipt were identified. As the flu vaccine is often offered at little to no cost, it may be unlikely that many families would delay or forgo a flu vaccine for their child due to cost. However, delaying or forgoing any type of care may have spillover effects on receipt of preventive services, including vaccinations, by reducing knowledge about preventive services and decreasing general access to health services. Reducing any type of unmet healthcare need for children and their family members may improve both short and long-term health outcomes for children by increasing their opportunity to receive timely and preventive care.

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EARLY CHILDHOOD OBESITY AND COGNITIVE ABILITY. *Amanda Brzozowski, Michael Kramer, Julie Gazmararian, Claire Coles, Carolyn Drews-Botsch (Emory University, Rollins School of Public Health, Atlanta GA 30322)

The prevalence of childhood obesity raises concern about the impact of obesity on child development. Data from the Follow-Up Development and Growth Experiences Study were used to assess the relationship between obesity and cognitive ability in 423 preschool-aged (4.5 years) children who had participated, as neonates, in a study of risk factors for small for gestational age. Using three measures (body mass index (BMI), triceps- and subscapular-skinfold-thickness (TST, SST)), obesity was defined as the top 15th percentile of CDC norms. Cognitive ability was estimated using the Differential Ability Scale (DAS, mean = 100, standard deviation = 15). Linear regression was used to examine the association between DAS score and obesity. Analyses defining obesity using skinfold measures were limited to boys since too few girls were identified as obese using these metrics. After adjustment, high BMI was associated with a non-significant decrease in composite (-3.61 points, 95% confidence interval (-8.58, 1.36)) and nonverbal (-4.34 (-10.01, 1.32)) DAS score among girls, but an increase among boys (3.89 (-4.66, 12.44) and 7.68 (-2.06, 17.42), respectively). BMI was not associated with verbal DAS scores and there was no association between high skinfold measurements and DAS scores. These findings suggest that obesity in early childhood may be associated with cognitive development, particularly non-verbal ability, but that the relationship may differ between boys and girls. However, caution should be used in interpreting these results, since BMI may reflect muscle, rather than fat accumulation. The observed results may represent an association between increased musculature and non-verbal development in boys, rather than a causal association between obesity and development.

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ASSOCIATION BETWEEN BETEL QUID CHEWING AND CHANGE IN CAROTID INTIMA-MEDIA THICKNESS IN RURAL BANGLADESH. *Tyler R McClintock, Fen Wu, Faruque Parvez, Weijia Wang, Tariqul Islam, Alauddin Ahmed, Rina Rani Paul, Ishrat Shaheen, Golam Sarwar, Ryan T Demmer, Moise Desvarieux, Habibul Ahsan, Yu Chen (New York University School of Medicine, New York NY 10016)

Betel nut is the fourth most commonly used addictive substance in the world. Though recent evidence suggests it may play a role in the development of cardiovascular disease, no studies have investigated whether betel nut use is related to preclinical atherosclerosis. We evaluated these parameters in a subset of participants enrolled in the Health Effects of Arsenic Longitudinal Study (HEALS). Betel nut use was assessed in baseline interviews conducted during two discrete enrollment periods (2000-2002, 2006-2008), wherein each participant was questioned about present and past use of betel quid, along with frequency and duration of use. Carotid artery intima-media thickness (IMT), a validated surrogate marker of preclinical atherosclerosis, was measured from 2010-2011 for 1206 participants randomly sampled from the HEALS. A significant positive association was observed between duration of betel nut use and IMT, with above median use (7 or more years) among betel chewers corresponding to a 19.0 μm (95% confidence interval [CI]: 5.0-33.0) increase in IMT ($p < 0.01$) after adjusting for age, sex, body mass index, education, systolic blood pressure, and cigarette smoking. This effect was more pronounced in men (32.8 μm; 95% CI: 7.0-54.0; $p < 0.01$). Cumulative exposure also corresponded with increased IMT, as above-median exposure (30 or more quid-years) increased IMT by 17 μm (95% CI: 3.0-31.0; $p < 0.01$) overall and by 31.0 μm (95% CI: 7.0-54.0; $p < 0.01$) in men. A synergistic effect was observed between cigarette smoking and betel use, with above-median betel use plus ever cigarette smoking associated with a 42 μm (95% CI: 22.0-63.0; $p < 0.01$) increase in IMT. These findings suggest that betel nut use at long duration or high cumulative exposure levels is associated with preclinical atherosclerosis as manifested through carotid IMT. This effect is especially pronounced among men and cigarette smokers.

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GENETIC AND PERIPHERAL BIOMARKERS FOR AMYLOID DEPOSITION IN THE BRAIN. *Timothy Hughes, Lewis Kuller, Emma Barinas-Mitchell, Rachel Mackey, Eric McDade, William Klunk, Chester Mathis, Steven DeKosky, Oscar Lopez (University of Pittsburgh, Pittsburgh PA 15213)

Background: Recent advances in positron emission tomography using amyloid specific ligands (e.g. Pittsburgh Compound B (PiB-PET)) have revolutionized Alzheimer's disease (AD) research by enabling the in vivo measurement of brain amyloid deposition. Methods: We studied 175 non-demented participants aged 83-96 from the Gingko Evaluation of Memory Study with PiB-PET in combination with potential AD risk factors including: genetic polymorphisms associated with AD; plasma biomarkers of peripheral inflammation, apolipoproteins (Apo), cholesterol and oxysterol metabolites of cholesterol; as well as, blood pressure (BP) and arterial stiffness using pulse wave velocity (PWV, $n = 92$) measured by the automated waveform analyzer. All participants underwent detailed neuropsychological battery and adjudication of cognition. Results: More than half (97/175) of non-demented elderly adults were PiB+ for high amyloid deposition in the brain. PiB+ status was: significantly associated with genetic markers related to cholesterol transport (ApoE-4, $p < 0.01$ and ABCA7, $p = 0.02$), low plasma ApoE levels ($p = 0.02$) and higher arterial stiffness (brachial ankle PWV, $p < 0.01$ and systolic BP, $p = 0.04$); marginally associated with high plasma ApoJ ($p = 0.10$), HDLc ($p = 0.17$) and variation in the ABCA1 gene ($p = 0.24$); but not associated (all $p > 0.48$) with total cholesterol, LDLc, triglycerides, diastolic BP, cholesterol metabolites, and variation in the CLU gene encoding ApoJ. Conclusions: This study identified several potential risk factors for amyloid deposition in the brain. There is strong evidence that changes in cerebrospinal fluid, brain amyloid and brain glucose metabolism are present many years before clinical diagnosis of dementia. The genetic, lifestyle and environmental determinants of these early abnormalities and subsequent interventions to prevent dementia are likely a new direction for dementia epidemiology research.

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IMPACT OF DIFFERENTIAL MISCLASSIFICATION ON THE ASSOCIATION OF METABOLIC SYNDROME WITH A TRIAL FIBRILLATION RISK: THE ARIC STUDY. *Alvaro Alonso, Alanna Chamberlain, Richard MacLehose (University of Minnesota, Minneapolis MN 55454)

Objective: To assess the impact of differential outcome misclassification in an epidemiologic study of atrial fibrillation (AF), a common cardiac arrhythmia, using probabilistic bias analysis. Methods: 15,094 participants from the Atherosclerosis Risk in Communities cohort initially free from AF were followed up from 1987-89 through 2005. Metabolic syndrome and other relevant covariates were assessed at baseline through questionnaires and a physical exam. Incident AF during follow-up was ascertained from hospitalization discharge codes and study electrocardiograms. A probabilistic bias analysis of outcome misclassification was conducted following the approach proposed by Lash et al (Pharmacoepidemiol Drug Saf 2010, PMID: 20535760), which corrects estimates of association applying a bias factor which is sampled repeatedly from a probability distribution. We assumed perfect specificity and specified the distributions for our sensitivity parameters as triangular distributions with min = 0.75, mode = 0.9, max = 1.0 in individuals with metabolic syndrome, and min = 0.5, mode = 0.75, max = 1.0 in those without it and applied to the hazard ratio (HR) obtained from a conventional Cox model. We drew 100,000 samples from these distributions and estimated 95% uncertainty intervals (UI), accounting for both random sampling error and the uncertainty in the sensitivity values using the 2.5th and 97.5th percentiles of the ranked corrected estimates. Results: Over an average follow-up of 15 years, 1238 AF events were identified. Baseline prevalence of metabolic syndrome was 41%. The conventional multivariable HR (95% CI) not adjusted for misclassification was 1.67 (1.49-1.87). Adjusting for differential outcome misclassification and random error the HR (95% UI) was 1.42 (1.01-1.89). Conclusion: Our results suggest that even a substantial degree of differential misclassification in AF diagnosis is unlikely to explain the association between metabolic syndrome and AF risk.

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TESTOSTERONE AND CARDIOVASCULAR RISK FACTORS IN MEN, A MENDELIAN RANDOMIZATION ANALYSIS IN THE GUANGZHOU BIOBANK COHORT STUDY. *Jie Zhao, Tai Hing Lam, Kar Keung Cheng, Bin Liu, Weisen Zhang, Chaoqiang Jiang, Gabriel M Leung, C Mary Schooling (The University of Hong Kong, Hong Kong SAR China)

Observationally lower testosterone is associated with an unhealthier cardiovascular (CVD) risk profile, but this association is open to confounding and reverse causality. The authors examined the association of testosterone with well-established cardiovascular disease risk factors (blood pressure, LDL-cholesterol, HDL-cholesterol and fasting glucose) and Framingham score using a Mendelian randomization analysis with a separate-sample instrumental variable (SSIV) estimator. To avoid reverse causality, a genetic score predicting testosterone was developed in 290 young Southern Chinese men from Hong Kong based on a parsimonious set of genetic polymorphisms from selected testosterone-related single nuclear polymorphisms (SNPs) (rs1008805, rs2175898, rs10046, rs1256031). Multivariable linear regression was used to examine the association of predicted testosterone with CVD risk factors and Framingham score among 4184 older Southern Chinese men from the Guangzhou Biobank Cohort Study. Predicted testosterone was not clearly associated with CVD risk factors: systolic blood pressure (0.78 mmHg, 95% confidence interval (CI) -10.89 to 12.45), diastolic blood pressure (2.80 mmHg, 95% CI -3.37 to 8.97), LDL-cholesterol (0.24 mmol/L, 95% CI -0.09 to 0.58), HDL-cholesterol (-0.15 mmol/L, 95% CI -0.34 to 0.04), fasting glucose (0.43 mmol/L, 95% CI -0.36 to 1.23) or Framingham score (0.04 score, 95% CI -0.37 to 0.45) per nmol/L higher predicted testosterone, after adjustment for potential confounders (age, education, smoking status, use of alcohol and body mass index). A Mendelian randomization analysis did not corroborate protective effects of testosterone on cardiovascular risk factors or risk of ischemic heart disease among men. Replication in a larger sample is required.

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PUBLIC SMOKING LEGISLATION AND HOSPITALIZATIONS FOR ISCHEMIC HEART DISEASE IN ATLANTIC CANADA, 1996-2010: MIXED-EFFECTS MODELING OF MULTILEVEL POPULATION HEALTH INTERVENTIONS. *Robert Hawes, Ken Johnson, Daniel Krewski (Institute of Population Health, Ottawa ON Canada)

Background: To reduce personal exposure to environmental tobacco smoke (ETS) and improve cardiovascular health, comprehensive public smoking legislation (PSL) has been enacted at the municipal and provincial levels in Atlantic Canada. The varying dates and geographic coverage of PSL in this region provide a unique opportunity to distinguish the effect of the intervention from other temporally plausible associations with ischemic heart disease (IHD). Objectives: To examine the implementation effects of PSL on hospital admissions due to IHD in Atlantic Canada 1996-2010, and to explore the contextual influences that impede or promote policy-based population health interventions. Methods: The level of protection and implementation date of 6 provincial and 14 local PSL were linked to 865 municipalities in four provinces using ArcGIS, along with Canadian census data and the adult smoking prevalence from seven national health surveys. 249,081 inpatient hospitalizations for IHD were extracted from the national Hospital Morbidity Database and tabulated by date for each municipality. Multilevel interrupted time-series Poisson regression was used to calculate the instantaneous and post-implementation effect of PSL on IHD hospitalizations, and to identify the correlates of successful PSL interventions. Results: The implementation of PSL contributed to 15,878 fewer hospitalizations for IHD in Atlantic Canada during the study period, equal to $149.2 million in health care costs saved. Median incidence rate ratios (MIRR) indicated substantial within-province variation in IHD following PSL, particularly in Newfoundland & Labrador (MIRR = 1.96) and New Brunswick (MIRR = 2.0). PSL is an efficient, equitable and cost-effective tool in reducing the population burden of IHD.

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METHODS USED TO EVALUATE POTENTIAL BIASES IN VACCINE PREGNANCY SAFETY STUDIES USING ELECTRONIC HEALTH DATA. *Gabriela Vazquez-Benitez, Elyse Olshen Kharbanda, James Nordin, Heather Lipkind, Allison Naleway (HealthPartners Institute for Education and Research, Minneapolis MN 55419)

Vaccines are increasingly targeted to women of reproductive age and two vaccines, influenza and pertussis, are specifically recommended during pregnancy. Pre-licensure clinical trials do not typically include pregnant women; when included, trials may not enroll enough pregnant women to detect rare events. Thus post-licensure vaccine safety assessments, utilizing electronic health care, are necessary. Our current work in the Vaccine Safety Datalink (VSD) has focused specifically on maternal and infant safety following exposures to vaccines during pregnancy. We have identified several potential challenges utilizing electronic health care data when analyzing exposure-pregnancy outcome associations. Our goal is to discuss specific issues related to cohort identification, timing and temporal trends of vaccination, confounding, and assessment of outcomes. Utilizing a subset of data from two ongoing studies of influenza vaccine safety during pregnancy (AJOG 2012, S47-51), we provide examples and demonstrate analytic strategies to address these issues. Specifically, we demonstrate that significant biases in the vaccine-outcome associations may occur if studies do not adequately adjust for seasonal trends in vaccination and health care utilization patterns. In addition, for maternal and perinatal outcomes, it is important to account for the time-dependency of exposures and outcomes. For example, women with preterm deliveries have less time while pregnant to be vaccinated. Observational studies using electronic health data for pregnancy safety studies must collect relevant covariates and address these potential biases in the analysis phase. Although our methodology has been developed conducting studies of vaccine safety, our findings are relevant across the field of perinatal and reproductive health.

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LOW-INCOME NEIGHBORHOODS AND VERY PRETERM BIRTH: AN APPLICATION OF CASE-CONTROL-WEIGHTED TARGETED MAXIMUM LIKELIHOOD ESTIMATION. *Michelle Pearl, Laura Balzer, Jennifer Ahern (Sequoia Foundation, Richmond CA 94804)

Although very preterm birth (VPTB) is a major contributor to infant morbidity and mortality, its underlying causes are poorly understood. Research suggests neighborhood socioeconomic conditions may contribute to preterm birth, and possibly VPTB. We aim to assess the relation between living in a low income neighborhood and VPTB (<32 weeks gestation) applying three estimation methods in a case-control setting. The California Very Preterm Birth study sampled cases and controls from a linked cohort of singleton live births delivered from 2000 to 2007 in southern California who participated in statewide prenatal screening; this analysis focuses on white mothers (428 cases and 200 controls). Neighborhoods of birth residence scoring below the median on an index of census tract income, poverty and public assistance levels were considered "low income." Marginal estimates of the risk difference (RD) and risk ratio (RR) were obtained through case-control-weighted targeted maximum likelihood estimation (CCW-TMLE) employing data-adaptive prediction of treatment and outcome mechanisms. For comparison, RR and RD were also estimated from non-targeted parametric maximum likelihood (CCW-MLE) and with a non-targeted data-adaptive algorithm, SuperLearner (CCW-SL). All estimators incorporated weights based on the known population prevalence of VPTB (0.63% among white women), and adjusted for age, education, parity, insurance and other neighborhood characteristics. The RD and RR associated with neighborhood low income under CCW-TMLE were 0.49% (95% confidence interval [CI]: 0.32%, 0.66%) and 2.05 (95% CI: 1.61, 2.60), respectively. CCW-MLE and CCW-SL estimates were similar. Results suggest a strong relation between low neighborhood income and VPTB among white women. However these estimates may differ from the true causal effect due to unmeasured confounding.

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OVERCOMING OBSTACLES TO PROBABILISTIC BIAS ANALYSIS APPLIED TO LARGE DATASETS. *Timothy Lash, Barbara Abrams, Lisa Bodnar (Deparment of Epidemiology, Rollins School of Public Health, Emory University, Atlanta GA 30322)

Probabilistic bias analysis uses Monte Carlo methods to address the direction, magnitude, and uncertainty of systematic errors potentially affecting an epidemiologic dataset. These methods require iterative application of a bias model to the original dataset, sometimes creating as many as 100,000 revised versions of the original data. Epidemiologic datasets can be quite large, particularly if based on population-wide registries or repeated measurements of a cohort over substantial follow-up time. In this case, the iterative manipulation and writing of 100,000 datasets may create an obstacle to probabilistic bias analysis, particularly when implemented on a desktop personal computer. We evaluated five strategies to overcome this obstacle, using an exemplar dataset of 940,000 birth certificates that included 4800 neonatal deaths as the outcome. The risk of neonatal death was associated with increasing maternal BMI after adjustment for seven potential confounders. BMI was likely misclassified on the birth certificates. Using previously published methods of Monte Carlo-based probabilistic bias analysis programmed in SAS to evaluate the bias from misclassification, we were unable to complete 100,000 iterations on a desktop PC. Neither adding a 2 terabyte accessory drive nor deleting the seven covariates from the regression model (with the intent of post-hoc adjustment for confounding) solved the memory limitation. We next implemented a case-cohort approach, sampling 2.5% of births as controls rather than including all 940,000, and then implementing the probabilistic bias analysis. Results were generated in 15.5 hours with 6 hours of processor time (as reported by SAS). Weighted regression, in place of a record-level dataset, offers a second feasible solution. We conclude that probabilistic bias analysis can be successfully applied to large datasets on conventional computing platforms, but special adaptions are likely to be required.

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SENSITIVITY ANALYSIS IN PREGNANCY OUTCOMES RESEARCH. *Kristin Palmsten, Krista F Huybrechts, Sonia Hernandez-Diaz (Harvard School of Public Health, Boston MA 02446)

Sensitivity analyses are used to assess the impact of bias on study results. Here we demonstrate an application to a pharmaco/perinatal epidemiology study. We identified a cohort of pregnancies from 2000-2007 US Medicaid healthcare data. Among the 100,942 women with depression, we calculated the relative risk (RR) and 95% confidence intervals (CI) for antidepressant (AD) use and risk for preeclampsia. AD use, either serotonin-norepinephrine reuptake inhibitor (SNRI) or selective serotonin reuptake inhibitor (SSRI), was identified by pharmacy records. Preeclampsia was identified by diagnostic codes. We corrected crude RRs for outcome misclassification as described by Lash et al. We corrected covariate adjusted RRs for unmeasured confounders, smoking and obesity, as described by Schneeweiss. The risk for preeclampsia among women with depression and no AD use was 5.4%. The crude preeclampsia RR was 1.6 (CI: 1.3-2.0) for SNRIs and 1.0 (CI: 0.9-1.1) for SSRIs. Assuming preeclampsia specificity was 98.5% and outcome misclassification was nondifferential, the bias corrected RR was 1.9 for SNRIs and 1.0 for SSRIs. If preeclampsia sensitivity was 5% lower in AD users than nonusers, the corrected RR was 2 for SNRIs and 1.1 for SSRIs. The adjusted preeclampsia RR was 1.5 (CI: 1.3-1.8) for SNRIs and 1.0 (CI: 0.9-1.1) for SSRIs. Assuming 40% of nonusers and 20-60% of users smoked, and the smoking-preeclampsia RR is 0.7, the corrected RR ranged from 1.4-1.6 for SNRIs and from 0.9-1.1 for SSRIs. Assuming 30% of nonusers and 20-50% of users were obese, and that the obesity-preeclampsia RR is 3.0, the corrected RRs ranged from 1.7-1.2 for SNRIs and from 1.1-0.8 for SSRIs. The primary SNRI association was probably biased downward due to outcome misclassification. Residual confounding by smoking and obesity likely had a minor impact on our results which is consistent with a previous study by Toh et al.

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ACKNOWLEDGING AND SATISFYING THE POSITIVITY ASSUMPTION IN CASE-CONTROL STUDIES. *Alan Kinlaw, Anna Maria Siega-Riz, Nancy Dole (University of North Carolina, Chapel Hill NC 27599)

Epidemiologic studies often violate the assumption of positivity which is essential to causal inference and is upheld when all observed strata of covariates contain exposed and unexposed individuals. Limited population size, finite biospecimen availability, or budget restrictions may restrict positivity. Potential lack of comparability between exposed and unexposed individuals threatens precision and validity, and can occur in case-control studies because controls are selected by outcome regardless of exposure status. Positivity, however, is independent of outcome and depends on variation of exposure within covariate strata. To ensure positivity in individually matched case-control studies analyzed using conditional logistic regression, all covariate values must be comparable within each matched set. We apply an illustrative example of limited positivity in a case-control analysis nested in the Pregnancy, Infection and Nutrition Study. To estimate the association between vitamin D level and preterm birth, 154 cases and 288 non-cases were matched individually by race, season and gestational age at serum draw. Other covariates included binary (smoking during pregnancy and chronic hypertension) and continuous variables (maternal age and education). Matched sets were *a priori* determined to uphold positivity if 1) smoking and hypertension were identical across exposure levels and 2) maternal age and maternal education were ≤6 and ≤4 years apart, respectively. 21% of matched sets satisfied criteria when all covariates were considered, and 64% were satisfactory when only smoking was considered. To uphold positivity under either criterion, high selection of satisfactory matched sets leads to suboptimal precision and potential for decreased internal validity. Controlling only for smoking induces bias by other known confounding factors. Study designs implementing countermatching and targeted matching may yield higher positivity in observational studies.

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LONGITUDINAL TARGETED-MAXIMUM LIKELIHOOD ESTIMATION (TMLE) OF THE EFFECT OF OCCUPATIONAL EXPOSURE TO PM2.5 ON THE INCIDENCE OF ISCHEMIC HEART DISEASE. *Daniel Brown, Sadie Costello, Mark Van der Laan, Maya Petersen, Mark Cullen, Ellen Eisen (UC Berkeley, Berkeley CA 94720)

Ambient exposure to fine particulate matter (PM2.5) is associated with heart disease in the general population but has rarely been evaluated in workplace studies. Occupational exposure to PM2.5, time-varying measures of health status, and incidence of ischemic heart disease were recorded in a cohort of 12,202 aluminum workers. Subjects were followed for 12 years unless censored by leaving work. The cohort was stratified by work process, fabrication versus smelting, due to differences in particle composition and job placement practices. A causal estimator was needed to adjust for confounding of the exposure-disease and censoring-disease relationships by time-varying health status. Longitudinal TMLE was used to estimate the cumulative incidence of heart disease that would result from workers being always exposed at levels above and below a specific PM2.5 cut-off, while remaining at work until retirement age. TMLE is doubly-robust to model misspecification of the exposure/censoring and outcome mechanisms, which were estimated with a cross-validated ensemble learner. Additionally, the TMLE is semi-parametric efficient in that it reaches the efficiency bound for estimators in minimal models corresponding to our causal assumptions if the likelihood components are consistently estimated. We discuss the theoretical and empirical aspects of the estimation procedure and present final estimates as adjusted survival curves. Results suggest that after 5 years of follow-up, the cumulative incidence of heart disease among smelter workers would be .083 if always exposed above the cut-off (.125 mg/m3) and .073 if always exposed below. Assessing the successive differences in cumulative incidence between exposure regimens provides evidence for the causal hypotheses about PM2.5 exposure and heart disease in these work environments.

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PROSTATE CANCER AND OCCUPATIONAL EXPOSURE TO WHOLE-BODY VIBRATION IN A NATIONAL POPULATION-BASED COHORT STUDY. *Marcella Jones, M Anne Harris, Paul A Peters, Michael Tjepkema, Paul A Demers (Occupational Cancer Research Centre; Dalla Lana School of Public Health, University of Toronto, Toronto ON Canada)

Previous work suggests that occupational exposure to whole-body vibration (WBV) may be associated with prostate cancer risk. This study used a large population-based cohort of working men to examine the relationship between WBV and prostate cancer and prostate cancer risk by Standard Occupational Classification 1991 category. The 1991 Canadian census cohort was linked by Statistics Canada to the national cancer registry (Canadian Cancer Database) and national vital statistics. For these analyses, the cohort was subset to working men aged 25-74 (n = 1,107,700). We assigned WBV exposure based on reported occupation in the 1991 census and previous expert assessments, then followed participants for incident prostate cancer until the end of 2003. Hazard rate ratios (HRs) and 95% confidence intervals (CI) were calculated using Cox proportional hazards modeling and adjusted for age, province of residence and socio-economic status. In men exposed to WBV, significantly elevated prostate cancer risk was observed in occupational category C (Natural & Applied Sciences) (adjusted HR = 1.37, 95% CI 1.09-1.72), and significantly reduced risk in category H (Trades, Transport & Equipment Operators) (adjusted HR = 0.91, 95% CI 0.86-0.97). Independent of exposure to WBV, small significantly elevated risks were seen in three occupational categories (A- Management, B- Business, Finance & Administrative, and I- Occupations Unique to Primary Industry) and significantly reduced risk was seen in one occupational category (H- Trades, Transport & Equipment Operators). We found no consistent relationship between WBV and prostate cancer. Further research could focus on specific exposures in the occupational categories we studied, as we did not measure exposure directly. Longer follow-up time may improve the power of future studies of prostate cancer risk by occupation in the Canadian population.

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PRE-MENOPAUSAL OCCUPATIONAL PHYSICAL DEMAND PROTECTS AGAINST HIP FRACTURES. *Aimee Palumbo, Yvonne Michael, Igor Burstyn, Brian Lee, Robert Wallace (Drexel University School of Public Health, Philadelphia PA 19102)

Bone fractures are a leading cause of disability, morbidity, and mortality and disproportionately affect older women. Few studies have examined the role of women's occupational exposure throughout the life course in relation to later life bone health. Data from the Women's Health Initiative Observational Study (n = 93,676), a long-term national cohort of women aged 50-79, were used to examine the association between physical demand in jobs outside the home, before and after menopause, and risk of hip fracture. At baseline, women reported age, duration, and description for up to three jobs held since 18 years of age, which were coded using the 2010 Standard Occupational Classification (SOC). A composite score summing multiple dimensions of physical demand was derived from the Occupational Information Network (O-Net) for each SOC code and applied to 88,927 women with complete occupational data. Duration and intensity of physical demand were calculated separately for pre- and post-menopausal time periods. Annual self-report of hip fracture was centrally adjudicated by medical record review; 2.35% of women experienced hip fractures during 8-10 years of follow-up. Poisson regression was used to estimate associations between physical demand and hip fracture. A 10-point increase in the intensity of physical demand during the pre-menopausal period was associated with 5% reduced risk of hip fracture (relative risk: 0.95, 95% confidence interval 0.92-0.99) after adjustment for age at study entry, body mass index, and ethnicity. No association between post-menopausal occupation and hip fracture was observed. These results suggest that occupational physical demand prior to menopause may protect against hip fractures later in life.

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USING MULTIPLE DATA SOURCES TO ENUMERATE WORK-RELATED AMPUTATIONS IN MASSACHUSETTS. *Kathleen Grattan, Lucy Bullock, Yaritza Roberts, Sangwoo Tak, Letitia Davis (Massachusetts Department of Public Health, Occupational Health Surveillance Program, Boston MA 02108)

The burden of work-related injuries is often estimated from a single data source; yet, no one source captures all cases and all characteristics of these cases. Massachusetts was one of three states funded by the Bureau of Labor Statistics to pilot multi-data source surveillance of work-related amputations and to examine the extent to which the Survey of Occupational Injuries and Illnesses (SOII), based on employer-reported injuries & illnesses, undercounts these amputations. Cases were compiled from four administrative data sets and the Massachusetts sample of the SOII. Data sets included workers' compensation records and three hospital data sets, collectively referred to as Case Mix (CM) data. Potential amputations were identified through injury classification codes (ANSI & OIICS), ICD-9 codes, and narrative searches. Medical records were abstracted to obtain worker/employer identifiers needed for case linkage. Work-related amputations were counted. Demographic/employment characteristics of these cases and the weighted sample of SOII-captured cases were contrasted. To address the SOII undercount, the subset of enumerated cases eligible for SOII was compared with the SOII estimate to compute amputation capture ratios. SOII underestimates public health burden of these amputations; multi-data source surveillance identified 577 (95% CI 525, 629) more amputations than estimated by the SOII (210, 95% CI 158, 262). This difference was only partially explained by amputation cases falling outside the scope of the SOII (e.g. the self-employed) and the finding that some amputations were reported as 'other injuries' in the SOII. Restricting enumerated cases to those clearly eligible for the SOII, the SOII estimate was 76% of the enumerated count yielding a 24% SOII undercount. Multi-source surveillance enhances our ability to characterize injuries but poses challenges not the least of which are differences in scope and coverage across data sources.

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OCCUPATIONAL PRESTIGE AND INFLAMMATION IN POSTMENOPAUSAL WOMEN. *Jolene Lee Masters Pedersen, Rikke Lund, Naja Hulvej Rod, Igor Burnstyn, Anneclaire De Roos, Candyce Kroenke, Lorena Garcia, Yuko You, Simin Liu, Yvonne L Michael (University of Copenhagen, Copenhagen Denmark)

While the link between socioeconomic status and health is well established, the mechanisms are less clear. This study estimated the association between occupational prestige and inflammation in women aged 50-79 years. We analyzed data from the controls in a nested case-control study of the Women's Health Initiative. Six markers of inflammation, C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), soluble intercellular adhesion molecule-1 (sICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and E-selectin were measured in 2,198 randomly selected women free from diabetes and cardiovascular disease. Women reported up to three jobs held longest since age 18, which were coded using the 2010 Standard Occupational Classification (SOC). Occupational prestige was assessed for each SOC code using the Occupational Information Network social status item, a standardized and occupation-specific descriptor ranging from 0 to 100. Multivariable linear regression was used to test the association of occupational prestige from the longest held job and inflammation adjusting for age, marital status and education. A ten unit increase in prestige score was associated with decreased inflammation; CRP (β 0.31;95% confidence interval -0.48,-0.13), IL-6 (-0.10;-0.23,0.03), TNF- α; (-29.78;-53.93,-5.62), sICAM-1 (-3.95;-6.82,-1.08), VCAM-1 (-4.10;-11.65,3.61), and E-selectin (-0.76;-1.39,-0.12). Occupational prestige merits further investigation as a plausible psychosocial mechanism linking socioeconomic status and adverse health outcomes.

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PRENATAL EXPOSURE TO DIETHYLSTILBESTROL AND REPRODUCTIVE HORMONES IN PREMENOPAUSAL WOMEN. *Lauren Wise, Rebecca Troisi, Elizabeth Hatch, Linda Titus, Julie Palmner, Alison Vitonis, Bernard Harlow (Slone Epidemiology Center, Boston University, Boston MA 02215)

Diethylstilbestrol (DES), a synthetic estrogen prescribed to pregnant women in the mid-1900s, is a potent endocrine disruptor. Prenatal DES exposure has been associated with infertility and other reproductive disorders in adult women, but little is known about its effect on endogenous hormones. Data were derived from the Harvard Study of Moods and Cycles, a prospective cohort study of women aged 36-45 years from Boston, MA (1995-1999). Prenatal DES exposure was reported at baseline via self-administered questionnaire. Early follicular-phase concentrations of follicle-stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (E2) were measured at baseline and every 6 months during 36 months of follow-up. Inhibin B concentrations were measured through 18 months. The analysis included 42 DES-exposed and 709 unexposed premenopausal women with intact ovaries. For each woman, hormone values were averaged over all time periods for which they were available; minimum and maximum values were identified. We used multivariable log-binomial and linear regression to estimate risk ratios (RR) and differences in mean log-transformed hormones (β), respectively, comparing DES-exposed with unexposed women. DES-exposed women had higher levels of FSH (IU/I) (average: β = 0.13, 95% confidence interval (CI): 0.00, 0.26; maximum: β = 0.20, CI: 0.05, 0.36) and lower levels of estradiol (pg/ml) (average: β = -0.18, CI: -0.31, -0.05; maximum: β = -0.22, CI: -0.39, -0.05) than unexposed women. Only maximum levels of LH (IU/I) were higher in the exposed (β = 0.23, CI: 0.05, 0.41). DES-exposed women had non-significantly lower levels of inhibin B (pg/ml) (average: β= -0.15, CI: -0.35, 0.05). RRs for the association of DES with average FSH > 10 IU/I and average inhibin B < 60 pg/ml, indicators of low ovarian reserve, were 1.84 (CI: 1.22, 2.76) and 2.09 (CI: 1.04, 4.22), respectively. These data suggest that prenatal DES exposure may influence reproductive hormones in late reproductive-aged women.

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PRENATAL EXPOSURE TO DIETHYLSTIBESTROL AND OBESITY IN MIDDLE-AGED WOMEN. *Elizabeth Hatch, Rebecca Troisi, Julie Palmer, Lauren Wise, Linda Titus, Winnie Ricker, Marianne Hyer, Robert Hoover (Boston University School of Public Health, Boston MA 02118)

Diethylstilbestrol (DES) is a non-steroidal estrogen that was commonly prescribed during pregnancy from the late 1940's to 1971. A potent endocrine disruptor, DES has been linked with reproductive tract malformations, cancer, infertility, and earlier menopause in prenatally exposed daughters. DES was used for years as a growth promoter in animal production, and animal studies suggest that DES may be associated with obesity. We used data from the National Cancer Institute DES Follow-up Study to evaluate the association between DES and obesity among 2927 prenatally exposed and 1396 unexposed women with confirmed exposure status. Weight and height were collected by mailed questionnaire in 2006; tape measures with instructions were sent to participants to record waist circumference (WC). We used multivariable log-binomial and linear regression to calculate risk ratios (RR) for obesity and mean differences (b) in body mass index (BMI) and waist circumference (WC), respectively, controlling for year of birth, education, parity and menopausal status. The RR for obesity comparing DES exposed with unexposed was 1.09 (95% confidence interval (CI):0.97, 1.22), and was similar in women who had never smoked (RR = 1.11, CI: 0.95,1.31). Among the ~40% with data on total dose, the RRs were 1.10 (CI: 0.89, 1.36), 1.26 (CI: 1.02, 1.55), and 1.26 (CI: 1.06, 1.50), for <2500, 2500-9999, and >10,000 mg of DES compared with no exposure. The RRs for obesity increased slightly with later gestational age at first exposure; RRs (CIs) were 0.98 (0.82, 1.18), 1.15 (0.97,1.37), 1.16 (0.96,1.39), and 1.20 (1.02,1.41) for first exposure at ≤7, 8-10, 11-14, and >15 weeks gestation, respectively, relative to no exposure. DES exposed women had slightly higher mean BMI (b = 0.30, CI: -0.12, 0.71), but differences in WC (cm) were minimal (b = 0.08, CI:-0.97, 1.13). This study suggests a small increase in BMI and obesity, but not in central adiposity, among prenatally DES-exposed women.

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IMPACT ON MATERNAL AND CHILD SERUM LEVELS OF PERFLUOROALKYL ACIDS OF IN UTERO AND LACTATIONAL TRANSFER. *Tony Fletcher, Debapriya Mondal, Rosana Weldon (London School of Hygiene and Tropical Medicine, London UK)

Measured maternal serum levels of perfluoroalkyl acids (PFAAs) have been associated with outcomes in children. Consideration of lactational exposure is important since changes in maternal serum levels by lactation may introduce confounding. The aim of the present study is to investigate the impact of pregnancy and breast-feeding on maternal and infant serum PFAA concentrations. 69,000 people from the mid-Ohio Valley, exposed to PFOA from industrial emissions, and typical US intake of other PFAAs, participated in a survey including blood samples in 2005-6. Among these 404 women were pregnant at survey, and were compared with non-pregnant; 633 had children aged 0-3 years in 2005-6 and reported their breastfeeding, for whom serum measures were available for 49 children. Attributable to pregnancy, we observed decreases in serum PFOA in pregnant compared to non-pregnant women: 19% decrease (95% CI: 5%, 30%) for the first trimester and 23% (11%, 33%) for the third. For PFOS decreases were not statistically significant. Due to lactation, we observed 34% (23%, 44%) and 26% (16%, 34%) decreases in maternal PFOA and PFOS levels, respectively, per 12 months breastfeeding and a stronger decreased effect of 60% (27%, 78%) for women with past, but not on-going, exposure to PFOA above the background level. For infants, serum levels in bottle-fed infants were similar to their mothers, but breastfeeding increased children's serum PFOA concentrations 2.0-fold (1.0, 3.0) and for PFOS 2.2-fold (1.4, 3.4). This study suggests that pregnancy and lactation significantly impact serum levels of PFAAs and in utero and lactational transfer are important exposure routes to infants. In studies where normal breast milk is a predictive factor for an outcome, there is a potential for confounding when considering environmental chemicals such as PFAAs carried in milk. Further, adjustment for lactation is needed when estimating in utero levels from serum measurements taken postnatally.

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MATERNAL SERUM PERFLUOROALKYL SUBSTANCES AND MATERNAL AND NEONATAL THYROID FUNCTION. *Yan Wang, Walter Rogan, Pau-Chung Chen, Guang-Wen Lien, Hsiao-Yen Chen, Matthew Longnecker, Shu-Li Wang (National Institute of Environmental Health Sciences, Research Triangle Park NC 27709)

Perfluoroalkyl Substances (PFASs) are organic compounds with hydrogen replacing fluorine on the carbon chain. They have been widely used in industrial and consumer products and are often detectable in humans. PFASs interfere with thyroid homeostasis in pregnant rats and their pups. In humans, maternal thyroid hormone supplies the fetus throughout pregnancy, and thyroid hormones play a critical role in fetal growth and neurodevelopment. Thus the present study was designed to investigate the associations between maternal PFAS exposure and thyroid function in pregnant women and neonates. In a study of health and environmental exposures in Taiwan, 241 pregnant women had serum concentrations of nine PFASs, thyroxin (T4), free T4, and thyroid stimulating hormone (TSH) measured in the third trimester and in cord serum. Associations between PFASs and thyroid function test results were examined in linear regression models with adjustment for potential confounders. Concentrations of maternal perfluorononanoic acid (PFNA), perfluoroundecanoic acid (PFUnDA) and perfluorododecanoic acid (PFDoDA) were inversely associated with free T4 levels in pregnant women; for example, there was a 0.8% decrease (95% CI: -30.6%, -9.5%) in maternal free T4 per ng/mL increase in maternal PFUnDA. Pregnant women with higher concentrations of perfluorooctanoic acid (PFOA) and perfluorohexanesulfonic acid (PFHxS) also had higher TSH levels. For example, maternal TSH increased 4.9% (95% CI: 0.1%, 9.9%) per ng/mL increase in maternal PFOA. Finally, maternal PFNA, PFUnDA and PFDoDA were also inversely related to neonatal total T4 levels in cord serum, for example, per ng/mL increase in maternal PFUnDA, neonatal total T4 declined 6.0% (95% CI: -10.0%, -2.0%). In conclusion, maternal serum concentrations of PFASs were associated with thyroid function test results in both pregnant women and neonates. However, the associations were subtle and of unclear clinical significance.

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MATERNAL MEDICATION AND HERBAL USE AND RISK FOR HYPOSPADIAS: DATA FROM THE NATIONAL BIRTH DEFECTS PREVENTION STUDY, 1997-2007. Jennifer Lind, *Sarah Tinker, Cheryl Broussard, Jennita Reefhuis, Suzan Carmichael, Margaret Honein, Richard Olney, Samantha Parker, Martha Werler (Centers for Disease Control and Prevention, Atlanta GA 30333)

We used data from the National Birth Defects Prevention Study, a multisite, population-based, case-control study, to assess maternal use of common medications and herbals during early pregnancy and risk for hypospadias. We analyzed data from 1,537 infants with second-or third-degree isolated hypospadias and 4,314 liveborn male control infants without major birth defects, with estimated dates of delivery from 1997-2007. Exposure was reported use of prescription or over-the-counter medications or herbal products, from 1 month before to 4 months after conception. Adjusted odds ratios (aORs) and 95% confidence intervals (CI) were estimated using multivariable logistic regression, adjusting for maternal age, race/ethnicity, education, pre-pregnancy BMI, previous live births, maternal sub-fertility, study site, and year. We assessed 64 medication and 24 herbal components. Maternal uses of most components were not associated with an increased risk of hypospadias. Two new associations were observed for venlafaxine (aOR 2.4; 95% CI 1.0, 6.0) and progestin only oral contraceptives (aOR 1.9, 95% CI 1.1, 3.2). The previously reported association for clomiphene citrate was confirmed (aOR 1.9, 95% CI 1.2, 3.0). Numbers were relatively small for exposure to other specific patterns of fertility agents, but elevated aORs were observed for the most common of them. Overall, findings were reassuring that hypospadias is not associated with most medication components examined in this analysis. New associations will need to be confirmed in other studies. Increased risks for hypospadias associated with various fertility agents raises the possibility of confounding by underlying subfertility.

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TRENDS AND DEMOGRAPHIC PATTERNS IN NON-MEDICAL USE OF PRESCRIPTION PIOIDS, 2002-2010. *Sam Harper, Jessica Adam-Smith, Nicholas B King (McGill University, Montreal QC Canada)

Accidental poisoning mortality from prescription opioid painkillers in the US has risen rapidly over the last decade, is socially patterned, and is possibly related to increases in non-medical use of these drugs. Few studies have examined time trends in non-medical use of prescription opioids, particularly differences by social group. We used data from the 2002-2010 National Survey of Drug Use and Health (n = 500914) to examine trends in non-medical use of prescription analgesics (including OxyContin), and the frequency of use by demographic subgroups. Past-year analgesic use remained stable (~5%) from 2002-2010, and we found no differential trends by demographic subgroup. Rates of use were higher for men, non-Hispanic whites, 16-25 year olds, the uninsured, and those with less than a 12th grade education. In contrast to overall analgesic trends, among analgesic users past-year use of OxyContin increased by 5 percentage points (10% to 15%) from 2004-2010, and the percentage point increase was greater for whites (6.6 points, 95% confidence interval [CI]: 3.7,9.6) and American Indians (21 points, 95% CI: -1.8,44.0). OxyContin use was consistently greater among those with lower income, men, 16-25 year-olds, and those without health insurance. In adjusted models, from 2004-10 OxyContin use increased from 11% to 23% among young, white, uninsured, low-educated men, but remained nearly constant at 8% for similarly-aged, well-educated, insured women. Among past-year analgesic users, whites and 16-34 year olds had higher likelihood of having obtained their last dose without a prescription. The probability of having obtained the last dose without a prescription was also 9.6 percentage points higher (95% CI: 6.4,12.7) among users vs. non-users of OxyContin. We found little increase in overall non-medical use of prescription analgesics, but changes in the composition of users reflect a shift towards the greater use of OxyContin, particularly among isadvantaged men.

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THE IMPACT OF TOBACCO CONTROL POLICIES ON DISPARITIES IN MATERNAL SMOKING DURING PREGNANCY. *Summer Sherburne Hawkins, Ariel Dora Stern, Christopher Baum (Boston College, Chestnut Hill MA 02467)

Disparities in maternal smoking during pregnancy continue to persist; however, population-level interventions to change behavior are limited. Using national birth files on all births in 29 states from 2000-2009 (N = 16,875,379), we assessed the impact of changes in cigarette excise taxes and smoke-free legislation on racial/ethnic and educational disparities in maternal smoking during pregnancy. We estimated probit differences-in-differences regression models with interactions between maternal race/ethnicity, education, and taxes as well as state- and year-fixed effects. The Tax Burden on Tobacco reports monthly cigarette excise tax for each state and Americans for Nonsmokers' Rights reports the date that state-wide smoke-free restaurant legislation took effect. From 2000-2009, maternal smoking during pregnancy decreased from 11.9% to 9.5%. Over this time period 28/29 states increased cigarette taxes, from 46 cents to $1.47, and 16/29 states saw smoke-free restaurant legislation come into effect. For every $1.00 increase in cigarette taxes, maternal smoking during pregnancy for white and black mothers with less than a high school degree decreased by 1.9 percentage points (adjusted Coefficient for both -0.019; p = 0.009). Among black mothers, cigarette taxes also decreased smoking across all educational levels. When analyses were repeated using the number of cigarettes smoked daily, we found that for every $1.00 increase in taxes, white and black mothers with less than a high school degree smoked approximately 18 fewer cigarettes per month. We found no effect of smoke-free legislation on maternal smoking during pregnancy. Cigarette taxes should be considered as an effective population-level intervention to reduce racial/ethnic and educational disparities in maternal smoking during pregnancy.

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NEIGHBORHOOD ALCOHOL OUTLETS AND THE ASSOCIATION WITH VIOLENT CRIME IN ONE MID-ATLANTIC CITY: THE IMPLICATIONS FOR ZONING POLICY. *Jacky Jennings, Adam Milam, Amelia Greiner, C Furr-Holden, M Debra, Frank Curriero, Rachel J Thornton (Johns Hopkins University, Baltimore MD 21224)

Violent crime such as homicide causes significant excess morbidity and mortality in U.S. urban areas. A health impact assessment (HIA) identified zoning policy related to alcohol outlets as one way to decrease violent crime. The objectives were to determine the relationship between alcohol outlets including off-premise alcohol outlets and violent crime in one urban area to provide local public health evidence to inform a zoning code rewrite. An ecologic analysis of census tracts in Baltimore City was conducted from 2011 to 2012. The data included violent crimes (n = 51,942) from 2006 to 2010, licensed alcohol outlets establishments (n = 1,327) from 2005 to 2006, and data on neighborhood disadvantage, percent minority, percent occupancy and drug arrests from 2005 to- 2009. Negative binomial regression models were used to determine the relationship between the counts of alcohol outlets and violent crimes controlling for other factors. Spatial correlation was assessed and regression inference adjusted accordingly. Each one-unit increase in the number of alcohol outlets was associated with a 2.2% increase in the count of violent crimes adjusting for neighborhood disadvantage, percent minority, percent occupancy, drug arrests and spatial dependence (Incident Rate Ratios (IRR) = 1.022, 95% CI = 1.015, 1.028). Off-premise alcohol outlets were significantly associated with violent crime in the adjusted model (IRR = 1.030, 95% CI = 1.014, 1.046). Baltimore City is in the midst of its first comprehensive zoning code re-write in forty years. Generating Baltimore-specific estimates of the relationship between alcohol outlets and violent crime has been central to supporting the incorporation of alcohol outlet policies in the rewrite.

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INFLUENCE OF GRANDPARENT SCHOOLING ON ADULT HEALTH STATUS, SMOKING, AND OBESITY. *Felice Le, Ana Diez Roux (University of Michigan, Ann Arbor MI 48103)

Background: Despite persistent education-related health inequalities in the U.S., little is known about multigenerational effects of schooling on adult health. As decreasing mortality rates make it more common for grandparents and grandchildren to share lifespans, direct influences of grandparent schooling on grandchild health may become increasingly important. Methods: We used multigenerational data spanning 41 years on a national sample of U.S. families to investigate influences on the global health, smoking, and obesity status of adults aged 25–55 years by their grandparents' educational attainment. We used marginal structural models to estimate direct effects of grandparent schooling unmediated by parent and participant schooling and accounting for confounders. Results: After accounting for parent and participant schooling, there were graded associations among Whites between higher grandparent schooling and lower prevalence of poor health status, current smoking, and obesity. Estimates among Blacks were similar to among Whites for smoking but minimal for health status and obesity. Estimated direct effects for health status and obesity were larger when the participant's highest educated grandparent lived in the same state. For example, the prevalence ratio (PR) of obesity for a grandparent with a college degree compared to less than high school = 0.66 (95% confidence interval 0.50–0.86) in same state vs. PR = 0.77 (0.59–1.01) in different state among Whites; PR = 0.91 (0.65–1.28) in same state vs. PR = 1.07 (0.76–1.51) in different state among Blacks. Conclusion: These results suggest that higher grandparent schooling may be beneficial for grandchild health in adulthood through pathways not mediated by parent and grandchild schooling, but that these benefits may be unequally distributed among racial groups. These differences may contribute to racial health disparities across generations.

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INNOVATIONS IN NEIGHBORHOOD RESEARCH: WHERE DO WE GO FROM HERE? *Claire Margerison-Zilko (University of Texas, Austin TX 78745)

Research on neighborhoods and health has grown exponentially in recent decades, with studies attempting to identify the effects of neighborhood socioeconomic status, built environment, social structure, and racial/ethnic makeup on outcomes such as cardiovascular disease, obesity, mental health, and birth outcomes. However, this research continues to be met with skepticism due to the inherent methodological challenges to making causal inference in this field. These challenges include: 1) appropriately defining neighborhoods, determining units of analysis, and measuring relevant neighborhood characteristics with respect to health outcomes; 2) accounting for individual-level factors that are associated with both neighborhood of residence and health outcomes and understanding interactions between individual and neighborhood characteristics; 3) going beyond cross-sectional designs to incorporate residential mobility and neighborhood change, and 4) accounting for selection of individuals into neighborhoods and the substantial stratification of neighborhoods with respect to socioeconomic status and racial/ethnic makeup in the US. In this symposium, we will hear from four researchers using innovative methods to address these challenges. These presentations will be followed by an interactive discussion in which we will delve further into the challenges and opportunities in the future of neighborhood research and attempt to answer the question: where do we go from here?

Speakers:

1. *Defining "neighborhood": exploring units of analysis and contributions of workplace neighborhood to cardiovascular risk* - Patricia O'Campo
2. *Navigating structural confounding/social stratification in neighborhood research* - Jennifer Ahern
3. *Interactions between individual- and neighborhood-level socioeconomic status in explaining racial/ethnic disparities in depressive symptoms during pregnancy* - Catherine Cubbin
4. *Beyond the cross-sectional: taking into account residential mobility and neighborhood change in neighborhood research* - Claire Margerison-Zilko

Discussant: Irene Yen

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INNOVATIVE DESIGN AND ANALYSIS ISSUES IN FETAL GROWTH STUDIES. *S Katherine Laughon (NICHD, NIH, Rockville, MD 20852)

Defining normal and abnormal fetal growth has not been straightforward. An international group of researchers will present the study design and clinically relevant motivation for methodological research in fetal growth on behalf of two ongoing longitudinal observational cohort studies, one in the United States (NICHD Fetal Growth Study) and another international (INTERGROWTH-21st). Innovative approaches for modeling fetal growth will be compared and contrasted with other approaches used for analyzing fetal growth longitudinal data. Methodological work focused on reference standard estimation and prediction of poor birth outcomes from longitudinal data with standard linear mixed modeling approaches will be presented. The robustness of standard approaches to modeling will be presented and more general approaches will be introduced that will be important for certain inferences and predictions. This session should be of interest to a wide range of epidemiologists, biostatisticians and clinician researchers including those interested in fetal growth, study design, model development, and analysis of longitudinal data.

Speakers:

1. *Study Design and Clinical Implications of the NICHD Fetal Growth Study* – S. Katherine Laughon (Epidemiology Branch, NICHD)
2. *Modeling Longitudinal Fetal Growth: The Development of a New Novel Approach with a Comparison with Existing Approaches* – Robert Platt (McGill University)
3. *Aspects of the Design and Analysis of the INTERGROWTH-21st Project to Develop Global Fetal Growth Reference Centiles* – Eric Ohuma (University of Oxford)
4. *Linear Mixed Models for Reference Curve Estimation and Prediction of Poor Pregnancy Outcomes from Longitudinal Ultrasound Data: Robustness to the Random Effects Assumption* –Paul S. Albert (Biostatistics & Bioinformatics Branch, NICHD)

Discussant: Una Grewal (Epidemiology Branch, NICHD)

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METHODOLOGICAL ISSUES IN PSYCHIATRIC EPIDEMIOLOGY. *Alyssa Mansfield, Jaimie Gradus (Department of Veterans Affairs, Honolulu, HI 96819)

Mental health issues are increasingly being studied as unique health outcomes, and included in larger studies of non-psychiatric primary outcomes as important factors contributing to other medical conditions. Compared with other disciplines, psychiatric epidemiological research involves special methodological challenges. This symposium will include presentations that highlight these challenges and outline available tools and approaches. Topics discussed will include: issues of measurement error & bias; causal inference; challenges associated with the use of the DSM and ICD diagnostic criteria; appropriately identifying risk factors of psychiatric outcomes, and assessing the effectiveness of interventions. Data from existing studies will be presented to highlight these issues and present potential solutions utilized in practice. This symposium brings together researchers with expertise in trauma, suicide, substance abuse, mood disorders and other mental health issues across the life course to discuss methodological issues that frequently arise in psychiatric epidemiology and how best to handle them.

Speakers:

1. *Challenges in Psychiatric Epidemiology: A Primer for All Epidemiologists*, Alyssa Mansfield, VA Pacific Islands Health Care System, National Center for PTSD
2. *Early Life Stress and Adult Psychiatric Disorders: Assessing Causation in a Sea of Correlation,* Katherine Keyes, Columbia University
3. *Conceptual versus Categorical Misclassification: Sexual Victimization and Suicide as a Motivating Example*, Jaimie Gradus, VA Boston Health Care System, Boston University
4. *Epidemiologic Approaches to Validating the Diagnostic Criteria and the Bereavement Controversy in the Diagnosis of Major Depression*, Stephen Gilman, Harvard School of Public Health
5. *Primary vs. Tertiary Prevention for Posttraumatic Stress Disorder: Insights from Simulation Approaches*, Magdalena Cerda, Columbia University

Discussant: Sandro Galea, Columbia University

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RACIAL DISPARITIES IN CANCER: FROM THE MOLECULAR TO THE MACRO-ENVIRONMENT. *Sarah S Cohen, Lisa Signorello (International Epidemiology Institute, Durham, NC 27701)

In the United States, variation in cancer incidence and mortality rates exist across racial/ethnic groups in ways that are complex and incompletely understood. Variation in known risk factors such as exposure to infectious agents and lifestyle choices such as smoking may help explain some cancer disparities. However, it is increasingly evident that in order to grasp the underpinnings of many cancer disparities, we need to recognize the potential contribution of a broad spectrum of factors that range from the micro (i.e., molecular) to the macro (i.e., geo-societal) level. In this symposium, we will examine multiple potential drivers of racial disparities in cancer, in a progression from the highly biological to the societal/contextual. In this way we hope to share current information on the state of cancer disparities research across disciplines and to inspire critical thinking regarding new research questions and the design of future studies.

Speakers:

1. *Symposium Introduction* - Lisa Signorello, Harvard School of Public Health
2. *Tumor molecular heterogeneity and breast cancer disparities* - Melissa Troester, University of North Carolina
3. *Overcoming Disparities in Lymphoma Outcomes: From Social Support to Novel Therapeutics* - Christopher Flowers, Emory University School of Medicine
4. *Accounting for context: social and built environment and disparities in cancer risk and outcomes* - Scarlett Lin Gomez, Cancer Prevention Institute of California

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VISIONARY EPIDEMIOLOGY. *Jay Kaufman, Allen Wilcox (McGill University, Montreal QC Canada)

Epidemiologists publish papers that rely on data, and graphical display of data is the most effective and compelling format for conveying this information. When graphs are properly conceived and artfully executed they appear simple and straightforward: data made into pictures. But such clarity seldom comes without effort, and a brief perusal of our journals suggests that far too few epidemiologists make this effort. Why does graphical practice in our field lag so far behind that seen in many other disciplines? Epidemiologists generally receive no formal training in this crucial area of scientific communication, and the results of this neglect can range from comic to catastrophic. For graphs to convey useful (and not misleading) information, the analyst must start with a clear understanding of the message to be conveyed, select data economically, and then give close thought to scale, proportion, choice of symbols, and labeling. Furthermore, there are no standard conventions for conveying complex epidemiologic concepts such as interaction or changes over time. The purpose of this symposium is to provide practical guidelines to epidemiologists in conveying their data and results visually, pointing out common pitfalls and suggesting criteria for assessing graphical displays.

Speakers:

1. *Intro and preliminary presentation of the issues*: Jay Kaufman and Allen Wilcox
2. *Pictures at an exhibition: Sixteen visual conversations about one thing* - Howard Wainer
3. *The Visual Display of Information: The Art of Numbers* - Alyssa Goodman

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VITAMIN D FOR PREVENTION OF CARDIOVASCULAR DISEASE, CANCER AND OTHER CHRONIC DISEASES: STATE OF THE SCIENCE VS. CURRENT RECOMMENDATIONS. *Elizabeth Bertone-Johnson, Jo Ann Manson (University of Massachusetts, Amherst MA 01003)

Vitamin D has been widely promoted to prevent chronic conditions including cardiovascular disease, cancer, and osteoporotic fracture. However, findings from recent observational studies and randomized trials have been discrepant, and several conflicting recommendations for vitamin D intake have been released from professional organizations in the past two years. For example, recommendations from the Institute of Medicine and the US Preventive Services Task Force do not support routine vitamin D supplementation, while the Endocrine Society endorses supplementation with >2000 IU/d for many segments of the population. This session will present findings from recent studies evaluating whether vitamin D may be beneficial in preventing cardiovascular disease and cancer and promoting bone health. Panelists will then discuss whether current public health recommendations are consistent with the scientific evidence, and identify key objectives and important design issues for future studies of vitamin D and chronic disease.

Speakers:

1. *Introduction* - Elizabeth Bertone-Johnson, ScD, University of Massachusetts
2. *Vitamin D and Cardiovascular Disease* - JoAnn Manson, MD, DrPH, Harvard Medical School
3. *Vitamin D and Cancer* - Edward Giovannucci, MD, DrPH, Harvard School of Public Health
4. *Vitamin D and Bone Health* - Clifford Rosen, MD, Maine Medical Center Research Institute

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METABOLIC SYNDROME AND OVARIAN CANCER IN THE UNITED STATES: A STUDY IN THE SEER-MEDICARE LINKED DATABASE. *Britton Trabert, Nicolas Wentzensen, Hannah P Yang, Louise A Brinton (National Cancer Institute, Rockville MD 20852)

Metabolic syndrome, a cluster of co-occurring metabolic factors, is associated with an increased risk of cardiovascular disease and linked to certain cancers, including breast and endometrial. Recent evidence suggests that ovarian cancer risk may be increased among obese women, but it is unclear whether an association extends to metabolic syndrome. We conducted a nested case-control study within the Surveillance, Epidemiology and End Results (SEER)-Medicare linked database to examine whether metabolic risk factors, individually or combined, were associated with ovarian cancer. Cases (n = 9,554) were women diagnosed with ovarian cancer between 1993 and 2007. Controls (n = 123,536) were a 5% sample of female Medicare enrollees residing in the same SEER-13 registry region as cases during the same time period. Metabolic syndrome was defined, in the three years prior to case diagnosis and a comparable time period in controls, using the revised National Cholesterol Education Program criteria (3 or more of the following: obesity, high blood pressure, elevated triglycerides, low HDL cholesterol, elevated fasting glucose; based on ICD-9-CM codes from inpatient/outpatient diagnoses). Odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression, adjusted for age, race, geographic region, smoking status and state buy-in status. On average, study participants were 77 years old and white. An increased ovarian cancer risk was associated with metabolic syndrome [OR (95% CI) 1.08 (1.01-1.15)] and its component factors, namely obesity [1.19 (1.08-1.31)], high blood pressure [1.24 (1.18-1.31)] and elevated triglycerides [1.19 (1.07-1.34)]. After adjusting for obesity, the increased risks for elevated blood pressure [1.23] and triglycerides [1.16] remained significant. Our findings, from a large population-based study of older women in the United States, support that metabolic syndrome and its component factors increase ovarian cancer risk.

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ARE THERE RACIAL DIFFERENCES IN FREE VITAMIN D LEVELS? *Kelly Hirko, Eric Rimm, Kenneth Mukamal, Qiuyin Cai, Lisa Signorello (Harvard School of Public Health, Boston MA 02115)

Racial differences in circulating levels of total 25-hydroxyvitamin D (vitamin D) are well documented, with blacks generally exhibiting significantly lower levels than whites. However, data is lacking on racial differences in free vitamin D, that which circulates unbound to vitamin D binding protein or albumin, and which may be more biologically available. We characterized racial differences in serum levels of total and free vitamin D among 832 black and 246 white participants of the Southern Community Cohort Study, aged 40-79, who enrolled from 2002-2009 in the southeastern US. Linear regression models were used to estimate racial differences in total and free vitamin D adjusting for sex, age, dietary intake of vitamin D, geographic ultraviolet B radiation levels, obesity, and physical activity. Whites had higher mean (± S.D.) levels of total vitamin D than blacks (21.5 ± 10.3 vs. 15.8 ± 8.6 ng/mL, respectively, $P < 0.001$), but blacks had higher mean levels of free vitamin D than whites (9.0 ± 6.1 vs. 6.0 ± 4.0 pg/mL, respectively, $P < 0.001$), due to substantially higher levels of vitamin D binding protein among whites (311.2 ± 119.2 ug/mL) than blacks (145.7 ± 93.5 ug/mL). In separate multivariate linear regression models, black race was associated with lower total vitamin D (-6.6 ng/mL; 95% confidence interval (CI): -5.4,-7.8) but higher free vitamin D (+2.5 pg/mL; 95% CI: +1.7, +3.3) compared with whites. Estimated ultraviolet B radiation exposure was a strong predictor of both vitamin D measures, and both measures showed similar seasonal fluctuations. In summary, we observed that the documented racial disparity in total vitamin D status was not reflected in the free (or unbound) measure of this hormone. It will be important to determine the implications of these results on studies of racial disparities in vitamin D-related diseases and to understand which measurement is the most predictive of future disease.

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PERIODONTAL DISEASE AND LUNG CANCER INCIDENCE IN THE WOMEN'S HEALTH INITIATIVE OBSERVATIONAL STUDY.

*Xiaodan Mai, Jean Wactawski-Wende, Michael LaMonte, Kathleen Hovey, Ngozi Nwizu, Jo Freudenheim, Mine Tezal, Frank Scannapieco, Andrew Hyland, Robert Genco (University at Buffalo, The State University of New York, Buffalo New York 14215)

Background: While there is some evidence that periodontal disease is positively associated with lung cancer, prospective studies in women are limited. Previous findings may reflect residual confounding by smoking. Methods: Prospective analyses were conducted in a cohort of 66,171 postmenopausal women (mean age = 68.8; 43.5% former and 3.9% current smokers) enrolled in the Women's Health Initiative Observational Study. Periodontal disease history (PDhx) was self-reported and 645 subsequent incident lung cancer cases occurred during an average 6.9 (SD ± 2.5) years of follow-up. Cox regression analysis was used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association of PDhx (prevalence of 26.1%) and incident lung cancer adjusting for smoking measures and other potential confounders. Results: Among all women, the association between PDhx and lung cancer risk was strong and significant in unadjusted analysis (HR = 1.70, 95% CI: 1.47- 1.97), and was attenuated but remained significant after adjusting for detailed smoking history including pack-years smoking, years since quitting (former smokers), second-hand smoke exposure, age, and other potential confounders (HR = 1.25, 95% CI: 1.06-1.48). In analyses restricted to never smokers, PDhx was not associated with lung cancer (HR = 0.97, 95% CI 0.64-1.51). However among ever smokers, there was a suggestion of a synergistic association when stratified jointly on tertiles (T) of pack-years smoking and PDhx (PDhx- = No; PDhx ± Yes): T1 (PDhx-: referent; PDhx + : HR = 0.995, 95% CI 0.50-1.97), T2 (PDhx-: HR = 1.97, 95% CI 1.32- 2.96; PDhx+ : HR = 3.16, 95% CI 2.05-4.87), and T3 (PDhx-: HR = 2.79, 95% CI 1.79-4.34; PDhx + : HR = 3.54, 95% CI 2.25-5.58). Conclusions: Periodontal disease was not independently associated with lung cancer in non-smoking postmenopausal women. Among smokers, the potential synergism between periodontal disease history and smoking on lung cancer should be further examined.

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EFFECTS OF ACCESSIBILITY OF DERMATOLOGY CLINICS ON LATE DIAGNOSIS OF MELANOMA.

*Loraine Escobedo, Crew Ashley, Cockburn Myles (University of Southern California, Los Angeles CA 90089)

Late diagnosis of melanoma is associated with poor disease prognosis. Factors that affect stage at diagnosis include socioeconomic status and accessibility of dermatology clinics (dermatologist density, types of healthcare setting, proximity to clinics). In breast cancer studies, accessibility to screening services is a significant predictor of stage at diagnosis. However, very few studies examine this factor in relation with melanoma. This study used geospatial methods to illustrate the geographical distribution of melanoma and improve access to melanoma screening services in Los Angeles County, California. We explored the association between accessibility of clinics and advanced presentation of melanoma. Patients diagnosed with melanoma between 1999 and 2011 were identified through the Los Angeles County Cancer Surveillance Program, the population-based Cancer Registry for the county. We examined two outcome measures: (1) stage of disease defined by the American Joint Committee on Cancer and (2) Breslow tumor thickness from pathology reports. To measure clinic accessibility, dermatology clinics were identified through the American Academy of Dermatology website. Information on types of insurance accepted and appointment wait-times were collected from the clinics through simulated patient phone calls. Each patient was linked to a clinic closest to his/her address at diagnosis. Travel distance and time between each patient-clinic link were calculated using the North American Association of Central Cancer Registries' shortest path calculator. Logistic regression was performed to measure the effect estimate of the explanatory variables on tumor stage/thickness at diagnosis. Study results support the need for spatial analyses to locate areas with poor access to care and initiate screening programs to address the rising incidence rates of invasive melanoma.

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ORAL HYGIENE AND RISK OF HEAD AND NECK CANCER.

*Jeffrey Chang, Jenn-Ren Hsiao, Chun-Yen Ou, Hung-I Lo, Cheng-Chih Huang, Wei-Ting Lee, Jehn-Shyun Huang, Ken-Chung Chen, Tung-Yiu Wong, Sen-Tien Tsai, Chia-Jui Yen, Yuan-Hua Wu, Wei-Ting Hsueh, Ming-Wei Yang, Shang-Yin Wu, Jang-Yang Chang, Kwang-Yu Chang, Yi-Hui Wang, Ya-Ling Weng, Han-Chien Yang, Chen-Lin Lin, Fang-Ting Wang (National Health Research Institutes, Tainan Taiwan)

Previous studies suggested that poor oral hygiene contributes to the development of head and neck cancer (HNC), although the results have been inconsistent. The current analysis examines the association between oral hygiene and HNC and whether this association is modified by the consumption of alcohol, betel quid, or cigarette and by the genetic polymorphisms of inflammation-related genes. Three hundred seventeen HNC cases and 298 controls were recruited from the department of otolaryngology. Interviews were conducted to ascertain information on dental care practice. Genotyping was performed for 6 single nucleotide polymorphisms in IL6, IL10 and PTGS2. The analysis showed that HNC risk was increased among those without regular dental visits (odds ratio (OR) = 2.9, 95% confidence interval (CI): 1.49-5.63) and those who brush teeth less than twice a day (OR = 1.51, 95% CI: 1.02-2.22). Combining regular dental visits, teeth brushing, and use of dental floss and mouthwash into a dental care score (range: 0-4, 4 = worst dental care), every 1 point increment of dental care score was associated with 1.6 times increase in HNC risk (OR = 1.61, 95% CI: 1.26-2.07). A significant positive association between dental care score and HNC was observed among regular alcohol drinkers (OR = 1.94, 95% CI: 1.40-2.69) but not among never or occasional drinkers (OR = 1.34, 95% CI: 0.90-2.02) (interaction P = 0.02). Multifactor dimensionality reduction analysis divided the study subjects into high- and low-risk group based on combinations of dental care score and IL6 rs1800796 genotypes. Compared to the low-risk group, the high-risk group had an OR of HNC = 2.18 (95% CI: 1.45-3.26). The current study observed a significant positive association between poor oral hygiene and HNC risk, which can be modified by alcohol drinking and the genetic polymorphism of IL6.

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IMMUNE-RELATED CONDITIONS AND SUBSEQUENT RISK OF BRAIN CANCER IN A COHORT OF MALE UNITED STATES VETERANS.

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Background: An inverse association between personal history of allergy and risk of brain cancer has been reported in case-control studies. Our objectives were to evaluate the associations of brain cancer risk with allergy/atopy and autoimmune disease, and to explore associations with diabetes and infectious/inflammatory disorders in a large cohort with medically diagnosed immune-related conditions recorded prior to diagnosis of brain cancer. Materials: We used the hospital discharge records of a cohort of 4.5 million male US veterans, of whom 4,383 developed primary brain cancer. Rate ratios (RR) and 95% confidence intervals (CI) were calculated using time-dependent Poisson regression, adjusting for age, calendar year, race, and number of hospital visits. RRs were further evaluated by latency of immune-related conditions, age, and race. Results: We found a significant trend of decreasing RRs for brain cancer with longer latency of allergy/atopy (P = 0.02), but not other conditions. RRs for allergy/atopy and diabetes preceding brain cancer by 10 or more years were 0.60 (95% CI: 0.43, 0.83) and 0.75 (95% CI: 0.62, 0.93), respectively. RRs for 2 or more immune conditions tended to be lower than 1 condition, although not significantly so. Chronic bronchitis was associated with significantly reduced risk, while Addison's disease, atrophic gastritis, chronic prostatitis, and mycoses were associated with significantly increased risk of brain cancer. Conclusions: This study lends further support to the inverse association with allergy/atopy and diabetes of long latency. Our findings provide new evidence for the association of specific infectious/inflammatory conditions and brain cancer that require replication in independent studies.

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PREDICTED VITAMIN D SCORE AND OVARIAN CANCER RISK IN TWO PROSPECTIVE COHORTS. *Jennifer Prescott, Elizabeth Poole, Kimberly Bertrand, Susan Hankinson, Shelley Tworoger (Brigham and Women's Hospital, Boston MA 02115)

Experimental and ecologic studies suggest that vitamin D may reduce ovarian cancer risk. While a single measure of plasma 25-hydroxyvitamin D [25(OH) D] was not associated with ovarian cancer in the Vitamin D Pooling Project, overweight women had significantly lower risk (P-interaction < 0.01). Studies of plasma 25(OH)D and ovarian cancer risk have been limited by a relatively small number of cases with pre-diagnostic blood samples. Therefore, we developed a score to predict circulating 25(OH)D levels. Within the Nurses' Health Study (NHS) and NHSII, we prospectively derived predicted vitamin D (pVD) scores based on known determinants of plasma 25(OH)D starting in 1986 and 1991, respectively. Average pVD was updated biennially to represent long-term exposure. Cox proportional hazards models, stratified by age, questionnaire cycle, and cohort, were fit to estimate relative risks (RR) and 95% confidence intervals (CI) for ovarian cancer overall and histologic subtypes associated with quintiles of pVD. We confirmed 591 incident ovarian cancer diagnoses over 2,095,207 person-years of follow-up. We did not observe an association between pVD and ovarian cancer risk (highest vs. lowest quintile RR = 0.99, 95% CI = 0.76–1.30; P-trend = 0.59); however, pVD was associated with reduced risk among women ≤50 years of age (RR = 0.62, 95% CI = 0.36-1.06; P-trend = 0.04) while there was no association for older women. Associations by menopausal status were similar to age stratified results. pVD was not significantly associated with ovarian cancer risk in either normal weight or overweight women. No association was observed between pVD and serous ovarian cancer risk, but a reduced risk was suggested for non-serous subtypes. Long-term vitamin D exposure, as assessed by pVD, was not associated with overall ovarian cancer risk, but was suggestively inversely associated in younger women. Risk was reduced for non-serous subtypes, which more commonly arise in younger, premenopausal women.

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VALIDATION STUDY OF HYPERMETHYLATED GENES ASSOCIATED WITH PROSTATE CANCER RECURRENCE. *Marni Stott-Miller, Elaine A Ostrander, Ziding Feng, Marina Bibikova, Brandy Klotzle, Jian-Bing Fan, Janet L Stanford (Fred Hutchinson Cancer Research Center, Seattle WA 98109)

DNA promoter hypermethylation leading to functional loss of tumor suppressor genes is a frequent epigenetic event in cancer. A major clinical challenge in prostate cancer (PCa) is distinguishing indolent from aggressive PCa, but DNA methylation studies for PCa prognosis have received little attention. We utilized the Infinium HumanMethylation 450 BeadChip to assess genome-wide DNA methylation profiles using tumor tissue from patients with clinically localized PCa treated with radical prostatectomy. We determined recurrence status based on: (1) PSA (2) use of secondary treatment (3) a positive bone scan, CT or MRI, or (4) PCa-specific mortality. The final dataset included 104 men with evidence of recurrence and 304 men with no recurrence. The Bioconductor package 'minfi' was used to normalize the data and identify differentially methylated positions. Genes shown to be associated with recurrence or features of aggressive disease (high Gleason score, metastasis, PCa death) in at least two prior studies were evaluated. We identified CpG sites in promoter regions for the following 14 genes: *GSTP1, APC, RASSF1A, RARβ, PTGS2, CD44, PITX2, RUNX3, HOXD3, GPR7, ABHD9, CDH13, ASC*, and *MDR1*. The number of CpG sites per gene ranged from 5 to 40, and we calculated a cutoff p-value for each gene by dividing 0.05 by this number. Significant hypermethylation in at least 50% of the identified CpG sites was observed for *ABHD9* (7 of 12 sites), *HOXD3* (10 of 11 sites), and *GPR7* (5 of 10 sites). Confirmatory evidence was strongest for *HOXD3* (lowest $p = 1.72 \times 10^{-6}$). These results validate the association between promoter hypermethylation of three candidate genes and PCa recurrence, and highlight the potential of DNA methylation biomarkers for identifying patients with more aggressive PCa.

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SPATIAL EPIDEMIOLOGY OF CANCER AND PFOA. *Veronica Vieira, Kate Hoffman, Tony Fletcher (University of California, Irvine, Irvine CA 92697)

The C8 Health Project was established in 2005 as a large cross-sectional survey of residents living near a DuPont Teflon-manufacturing facility in Parkersburg, West Virginia. The DuPont facility released perfluorooctanoic acid (PFOA, C8) into the environment via aerial emission and discharge into the surface and groundwater. As a result, there was extensive contamination of the local drinking water, and the highest measured PFOA levels were in the Little Hocking Water Association (Ohio). The objective of this study was to assess the spatial distribution of cancer risk in the exposed Ohio community. Participants of the C8 Health Project were linked to the Ohio Cancer Incidence Surveillance System to identify cancer cases diagnosed from 1996 through 2005. Two controls per case were selected from among the survey participants and matched on year of birth and gender. We used generalized additive models to simultaneously smooth location and adjust for risk factors. Hypothesis testing was done with permutation tests. Analyses were adjusted for year of birth, race, body mass index, smoking, alcohol consumption, and whether the participant was employed by DuPont. We used the survey residential history to account for latency. The resulting models allowed us to predict continuous crude and adjusted log odds for the entire study area. There were sufficient case numbers to perform spatial analyses of breast and prostate cancers, two cancers that have been inconsistently linked to PFOA in some epidemiologic studies. We compared maps with and without adjustment for measured PFOA serum to assess whether spatial patterns could be explained by PFOA exposure, and there was no variation between the analyses. Although areas of increased breast cancer risk were observed, they were not statistically significant and were not located in regions with the highest PFOA exposure. Prostate cancer risk was higher closer to the facility but not statistically significant.

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HORMONAL CONTRACEPTION AND CERVICAL INTRAEPITHELIAL NEOPLASIA AMONG KENYAN WOMEN WITH HIV. *Hannah Leslie, Deborah Karasek, Laura F Harris, Emily Chang, Naila Abdulrahim, May Maloba, Megan Huchko (University of California, Berkeley, Berkeley CA 94720)

Background: Human immunodeficiency virus (HIV)-positive women are at increased risk for infection with human papillomavirus infection and development of cervical cancer. Limited research addresses the risk profile of this population, including if the association of hormonal contraceptives with cervical cancer documented in population studies and supported by animal research holds true. We used causal inference analytic methods to assess the effect of combined oral contraceptive (COC) use on diagnosis of cervical intraepithelial neoplasia 2 or greater (CIN2+) among Kenyan women with HIV. Methods: Women at three HIV clinics in Kisumu, Kenya were offered screening using visual inspection with acetic acid alone or in sequence with Lugol's iodine. Positive tests led to colposcopy and biopsy for diagnosis. Those reporting COC use during any clinic visit prior to screening were classified as exposed. Covariates, including age, education, marital status, gravidity, smoking, and CD4+ count nadir, were extracted from medical records and considered for inclusion based on a proposed structural causal model. We estimated the population-level association of COC with CIN2+ using three non-parametric, data-adaptive methods: simple substitution, inverse probability of treatment weighting, and targeted maximum likelihood estimation (TMLE). Results: Of 3,185 women screened and followed per protocol, 287 (9.0%) were diagnosed with CIN2+. Exposing all women to COC compared to all unexposed was associated with a 2.9% (95% confidence interval [CI] 0.1%, 6.9%) increase in prevalence of CIN2+ (TMLE results). Conclusion: Marginal modeling of COC use and CIN2+ supports increased risk due to hormonal contraception. Important limitations of this finding include time-dependent confounding and incomplete data on covariates such as women's sexual history and past COC use. Nonetheless, these findings suggest important further avenues of research for this high-risk population.

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ENDOMETRIOSIS AND RISK OF OVARIAN AND ENDOMETRIAL CANCERS IN THE NURSES' HEALTH STUDY II. *Elizabeth Poole, Wayne Lin, Marina Kvaskoff, Shelley Tworoger, Kathryn Terry, Stacey Missmer (Brigham and Women's Hospital and Harvard Medical School, Boston MA 02115)

Introduction: Endometriosis has been linked to ovarian cancer, but the association with endometrial cancer is unclear. Most epidemiologic studies use self-reported endometriosis (SRE), but endometriosis is frequently misreported. Further, endometriosis diagnosis can be delayed up to 7 years after symptom onset and may influence subsequent oral contraceptive use and reproductive outcomes. Thus, investigating endometriosis requires careful evaluation of endometriosis and confounders. In the Nurses' Health Study II, we collect both SRE and laparoscopically-confirmed endometriosis (LCE) and confounders every 2 years. Methods: We used Cox proportional hazards regression to estimate the relative risk (RR) and 95% confidence intervals (95% CI). We compared several models: 1) SRE vs. LCE; 2) lagging endometriosis diagnosis date to account for delayed diagnoses; 3) using covariates prior to diagnosis; and 4) a combination of 2 and 3. Results: Both SRE (RR: 1.82; 95% CI: 1.28-2.59) and LCE (RR: 2.15; 95% CI 1.47-3.14) were strongly related to risk of ovarian cancer. Endometriosis was not associated with endometrial cancer (SRE RR: 0.78; 95% CI: 0.42-1.44; LCE RR: 0.76; 95% CI 0.35-1.64). When LCE diagnosis was lagged, RRs were similar to non-lagged analysis. However, when using pre-diagnosis covariates, LCE RRs were attenuated for both ovarian (RR: 2.01; 95% CI: 1.37-2.94) and endometrial cancer (RR: 0.82; 95% CI: 0.38-1.77). The RRs were further attenuated when both LCE diagnosis and covariates were lagged, although the association with ovarian cancer remained statistically significant. Conclusion: For both cancer outcomes, lagging endometriosis diagnosis date and confounders resulted in attenuated associations, suggesting that the original analysis had inflated RRs due to misclassification and confounding by indication. Future explorations of the association between endometriosis and chronic disease risk should take these factors into account.

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SOY ISOFLAVONE INTAKE AND BONE MINERAL DENSITY IN BREAST CANCER SURVIVORS. *Michelle Baglia, Kai Gu, Xianglan Zhang, Ying Zheng, Peng Peng, Ping-Ping Bao, Wei Lu, Xiao-Ou Shu (Vanderbilt University, Nashville TN 37203)

Low bone mineral density (BMD) is common in breast cancer survivors due to acute estrogen deprivation which increases the risk for rapid bone loss and bone fracture. Soy food is a rich source of phytoestrogens known to have both estrogenic and anti-estrogenic effects. No study has been conducted to evaluate the association between soy food intake and BMD in breast cancer survivors. Forearm BMD was measured for 1699 participants of the Shanghai Breast Cancer Survival Study at 60 months post breast cancer diagnosis using dual energy x-ray absorptiometry. Soy food intakes collected at 6-, 18-, and 36-months post-diagnosis were averaged. Linear and logistic regressions were used to evaluate the associations of soy protein and isoflavones with BMD and osteoporosis. Confounding and effect modification by hormonal related factors such as menopausal age, years since menopause, body mass index (BMI), and tamoxifen use, were evaluated. The averaged mean (±SD) intakes of soy protein and isoflavones were 12.1 ± 6.5 grams/day and 48.2 ± 28.0 milligrams/day. Soy protein and isoflavone intakes were inversely associated with BMD and positively associated with osteoporosis at the proximal forearm; compared to the lowest quartile, the highest quartile of soy isoflavone intake was associated with a reduction of BMD by 0.0140 (95% confidence interval (CI): -0.0258, -0.0022) and an increased odds ratio of 1.65 for osteoporosis (95% CI: 1.06, 2.55). No effect modification by tamoxifen use or BMI was observed. Overall, our study suggests that soy isoflavone intakes at a median level of 79.5 milligrams/day (range: minimum - 99% = 62.6 - 174.3) may unfavorably affect BMD among breast cancer survivors.

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METABOLIC SYNDROME AND DEVELOPMENT OF ORAL NEOPLASMS. *Rebecca Hsieh, Ming-fang Yen, Hsiu-hsi Chen, Athanasios Zavras (Columbia University, Mailman School of Public Health, New York NY 10032)

Oral neoplasms are one of the most common cancers worldwide. Early asymptomatic oral premalignancy (OPM), including oral submucous fibrosis, homogeneous and non-homogeneous leukoplakia, and erythroplakia are precursors to oral cancer. Previous cross-sectional studies have noted an association between metabolic syndrome (MetS) and OPM prevalence, but no prospective cohort study has shown a clear association between MetS and OPM incidence. Using a cohort study of 72,482 subjects aged 20 years or older from the Keelung Community-based Integrated Screening program in Taiwan between 2003 and 2008, we investigated the relation between MetS and OPM incidence adjusting for known risk factors specific to the population such as areca nut chewing. Results from the Poisson regression model showed that the incidence rate of OPM among those with MetS (319.6 per 105) was significantly higher than those without MetS (160.0 per 105) (Rate Ratio = 2.00, 95% CI: 2.01, 2.95). After adjusting for age gender, smoking, alcohol drinking, and areca nut chewing, the incidence rate of OPM among those with MetS was still significantly higher compared to those without MetS (Rate Ratio = 1.67, 95% CI: 1.19, 2.35). Overall, we demonstrated a positive temporal association between MetS and OPM, independent of other well-known risk factors. Though future longitudinal studies should be conducted to assess the association between MetS and oral cancer, the association between MetS and OPM underscores a potential role of comorbid disorders in premalignant lesions. This finding may inform further prevention programs aimed at decreasing disease burden of OPM and potentially decreasing the development of oral neoplasms.

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META-ANALYSIS OF CYTOCHROME P450 2D6 INHIBITION AND BREAST CANCER OUTCOMES IN TAMOXIFEN-TREATED PATIENTS: NEW PERSPECTIVES ON AN ONGOING CONTROVERSY. *Deirdre Cronin-Fenton, Per Dankier, Timothy Lash (Department of Clinical Epidemiology, Aarhus University, Aarhus, Denmark)

Adjuvant tamoxifen treatment of estrogen receptor positive breast cancer reduces the rate of recurrence by about one-half. Genetic or drug-induced inhibition of cytochrome P450 2D6 (CYP2D6) reduces the serum concentration of tamoxifen's most active metabolites. Some have advocated for the use of CYP2D6 genetic testing in clinical practice, but no guideline recommends CYP2D6 genotyping. We conducted a qualitative review and quantitative meta-analysis of the clinical epidemiology studies to investigate the association of CYP2D6 inhibition and breast cancer recurrence. We searched for the terms "tamoxifen" and "CYP2D6" in PubMed, including all papers and abstracts through 31 January 2013 on the association of CYP2D6 gene variants or drug-drug interactions and the risk of breast cancer recurrence or mortality. We included 30 and 12 papers on genetic or drug-induced inhibition, respectively. We used random-effects meta-analytic models to generate summary effect estimates (EE) and associated 95% confidence intervals (95% CI) and funnel plots to assess publication bias. We generated 4 meta-analytic models: (1) weak CYP2D6 inhibitors such as citalopram (2) strong CYP2D6 inhibitors such as paroxetine (3) any reduced function allele, and (4) two reduced function alleles. The summary EE associating breast cancer recurrence with concomitant use of tamoxifen and a weak CYP2D6 inhibitor was 1.05, 95% CI = 0.91, 1.22; that of a strong CYP2D6 inhibitor was 1.03, 95% CI = 0.86, 1.23. The summary EE associating recurrence with inheritance of any reduced function allele was 1.38, 95% CI = 1.10, 1.73; that of two reduced function alleles was 2.08, 95% CI = 1.40, 3.10. Individual results were widely heterogeneous and the heterogeneity is not easily explained. Important design flaws were identified for some positive studies. Weakly positive summary associations between CYP2D6 inhibition and breast cancer recurrence are dominated by poorly designed studies.

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EPIDEMIOLOGY OF LUNG CANCER IN MOROCCO. *Hinde Hami, Abdelhafid Ayoujil, Faouzi Habib, Abdelmajid Soulaymani, Abdelrhani Mokhtari, Ali Quyou (Laboratory of Genetics and Biometry, Faculty of Sciences, Ibn Tofail University, Kenitra, Morocco)

Introduction: Lung cancer is one of the most common cancers in the world. It is a leading cause of cancer death in both men and women. The aim of this study is to determine the epidemiological characteristics of lung cancer in Morocco. Methods: A descriptive retrospective study of lung cancer cases diagnosed and treated at Al Azhar Oncology Center in Rabat between 1994 and 2004, was conducted. Results: During the period of study, 376 cases of lung cancer were diagnosed; 332 (88.3%) in men and 44 (11.7%) in women, giving a male-female ratio of more than 7 and representing 5.3% of all new cases of cancer reported during this period. The average age at diagnosis was 58 years. Lung cancer is strongly related to age with only 4.7% of cases diagnosed in persons younger than 40 years, 85% in those aged 40-74 years and 10.2% in those aged 75 years and over. Among all detected cases, 20.5% are metastatic at diagnosis and 142 (37.8%) died from lung cancer during the study period, accounting for 12.4% of all cancer deaths. Conclusions: In developing lung cancer prevention strategies, certain groups warrant particular attention. Steps need to be taken to reduce the high lung cancer incidence rates.

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FIFTEEN-YEAR EFFECTS OF HELICOBACTER PYLORI TREATMENT ON GASTRIC CANCER INCIDENCE AND MORTALITY AMONG PARTICIPANTS WITH DIFFERENT BASELINE GASTRIC LESIONS AND AGES. *Wen-Qing Li, Lian Zhang, Jun-Ling Ma, Linda Brown, Ji-You Li, Lin Shen, Kai-Feng Pan, Wei-Dong Liu, Yuanreng Hu, Zhong-Xiang Han, Susan Crystal-Mansour, David Pee, William Blot, Joseph Fraumeni Jr, Wei-Cheng You, Mitchell Gail (Department of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Rockville MD 20852)

Helicobacter pylori (H. pylori) infection is an established risk factor for gastric cancer (GC). In 1995, a large intervention trial was initiated in Linqu, Shandong Province, China; 2258 H. pylori-seropositive subjects were randomly assigned to receive H. pylori treatment (amoxicillin and omeprazole) or its placebo for 2 weeks. Our previous report has indicated a significant 39% decrease in GC incidence and a non-significant 33% reduction in GC mortality associated with H. pylori treatment after 14.7-years (1995-2010). Here we evaluated the effect of H. pylori treatment in subgroups defined by age and precancerous gastric lesions at baseline. We used conditional logistic regression to estimate the odds ratio (OR) of GC incidence and the Cox proportional hazards model to estimate the hazard ratio (HR) of GC mortality. The analyses revealed a significant decrease in GC incidence (OR = 0.56, 95% confidence interval (CI) = 0.34-0.91), and a non-significant decrease in GC mortality (HR = 0.63, 95% CI = 0.29-1.37), associated with H. pylori treatment, among those with advanced gastric lesions (intestinal metaplasia or dysplasia), but not among those with normal or mild gastric lesions. There was a favorable effect of H. pylori treatment on GC incidence (OR = 0.36, 95% CI = 0.16-0.79) and mortality (HR = 0.26, 95% CI = 0.09-0.78) among participants with baseline age ≥55 years, but not among those <55 years. H. pylori infection causes atrophy and has been shown to act early in gastric carcinogenesis in previous studies. Here we further observed favorable effects of H. pylori treatment among those with advanced gastric lesions or at advanced ages, which suggests late-stage effects of continued H. pylori infection in gastric carcinogenesis. Our failure to find an effect of H. pylori treatment among younger subjects or those with early stage gastric lesions may be in part due to the small numbers of incident GC cases in these groups or longer latency from mild lesions to GC.

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TOTAL AND IONIZED CALCIUM CONCENTRATIONS AND FATAL PANCREATIC CANCER. *Halcyon Skinner, Ronald Gangnon, Gary Schwartz (University of Wisconsin - Madison, Madison WI 53726)

Background: In prospective studies, high-normal concentrations of serum calcium (high normocalcemia) have been associated with a higher risk for fatal prostate cancer and for ovarian cancer. These associations may be due to the expression of parathyroid hormone related protein (PTHrP), the primary agent of humeral hypercalcemia of malignancy, by prostate and ovarian tumors. Because pancreatic cancers also express parathyroid hormone related protein (PTHrP), we reasoned that higher serum calcium may be associated with higher risk for pancreatic cancer. Methods: We used Cox proportional hazards models to evaluate associations between risk for pancreatic cancer and serum concentrations of total, albumin-adjusted, and ionized serum calcium using data from the Third National Health and Nutrition Examination Survey (NHANES III) and the 2010 mortality linkage file. Analyses accounted for the complex sampling design and survey weights used in NHANES III. Results: There were 32 deaths from pancreatic cancer among 14,198 participants over 2,292,331 person-years of follow-up. For those who died from pancreatic cancer, calcium was measured, on average, 8.8 years prior to death. After adjusting for age, height, body mass index, cigarette smoking status, and serum 25-hydroxy vitamin D levels, the risk for fatal pancreatic cancer increased 1.4 fold for each 0.1 mmol/L increase in total serum calcium (RH = 1.37; 95% C.I. 1.12 – 1.67) and 2.3 fold for each 0.1 mmol/L increase in ionized serum calcium (RH = 2.37; 95% C.I. 1.10 – 5.10). Results for albumin-adjusted calcium were similar to total serum calcium. We observed no association between serum 25-OH-D and pancreatic cancer risk. Conclusions: This is the first report of a prospective positive association between serum calcium measurements and pancreatic cancer. These findings suggest either that high normocalcemia increases susceptibility to pancreatic cancer or that it is a biological marker of underlying pancreatic malignancy. Our results require confirmation in other cohorts.

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THE EFFECT OF EXTREME HEAT DURING SUMMER ON PRETERM BIRTH AMONG NEWBORN BABIES IN NEW YORK STATE, 1991-2006. *Aida Soim, Shao Lin, Syni-An Hwang (New York State Department of Health, Albany NY 12237)

The relationship between meteorological factors and preterm birth is not well understood. Few studies have examined the effect of high ambient temperatures during the warm season on preterm birth. The objective of this study was to assess the association between extreme heat events and preterm birth. Using a case-control study design, cases were defined as singleton preterm births (gestational age less than 37 completed weeks). Controls consisted of a random sample of singleton, term babies born within the same years. Cases and controls were born in 10 New York State weather regions between 1991 and 2006. Two heat wave (HW) indicators were assigned for each region: 1) at least 3 consecutive days with maximum temperature 900F or above (HW90); 2) at least 2 consecutive days with maximum temperature equal or above the 97th percentile of the maximum temperature distribution (HW97). HW frequency and duration were also examined. Exposure odds ratios (OR) and 95% confidence intervals (CI) were calculated using logistic regression, while controlling for other weather factors, air pollution, and maternal socio-demographic variables. Both HW97 and HW90 were consistently associated with preterm birth if exposure occurred in the 3rd trimester of the pregnancy (OR = 1.03, 95% CI: 1.01, 1.05 and OR = 1.05, 95% CI: 1.02, 1.08 respectively). Exposure during the 3rd trimester to one HW97 resulted in OR = 1.02, 95% CI: 1.00, 1.04 while exposure to two or more HW97 yielded an OR = 1.10, 95% CI: 1.03, 1.17. No dose-responses for HW90 frequency and duration were observed. Extreme heat events during pregnancy may be associated with preterm birth with the strongest effect if the event occurred in the 3rd trimester of pregnancy.

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PRENATAL EXPOSURE TO ORGANOPHOSPHATE PESTICIDES AND RECIPROCAL SOCIAL BEHAVIOR IN CHILDHOOD.

*Melissa Furlong, Stephanie Engel, Dana Barr, James Wetmur, Mary Wolff (University of North Carolina, Chapel Hill NC 27510)

Prenatal exposure to organophosphate pesticides (OPs) has been associated with poorer neurodevelopmental outcomes in childhood, including low IQ, Pervasive Developmental Disorder (PDD), attention problems and ADHD. We investigated the relationship between biomarkers of prenatal OP exposure and impaired reciprocal social behavior in childhood, as measured by the Social Responsiveness Scale (SRS). Using a multi-ethnic urban prospective cohort of mother/infant pairs in NYC (n = 136) we examined the relation between prenatal maternal urinary levels of OP metabolites (diethylphosphates, dimethylphosphates, and total dialkylphosphates) and SRS scores at 7-9 years of age. Using generalized linear models and considering race, education, marital status, maternal age, smoking during pregnancy, and child sex as potential confounders, we found that SRS scores did not differ across tertiles of OP metabolite exposure (nM/gCre) (DAP tertile 1 SRS mean= 51.97 [95% CI 48.60 -55.34], DAP t2 = 52.16 [CI 49.15, 55.16], DAP t3 =51.64 [CI 48.67, 54.60]). We saw similar results for DEP tertiles (t1 = 50.78 [CI 47.62, 53.93], t2 = 51.21 [CI 48.14, 54.27], t3 = 53.52 [CI 50.54, 56.50]) and DMP tertiles (t1 = 53.19 [CI 49.92, 56.47], t2 = 52.02 [CI 48.89, 55.14], t3 = 51.25 [CI 48.24, 54.26]). We also examined the linear relationship between log-OP metabolites (adjusted for urinary creatinine) and SRS scores and found no association (DAP Beta = -0.94 [CI -3.68, 1.80]; DEP beta = 1.11 [CI -1.61,3.84]; DMP beta =-1.02 [CI -3.34, 1.31]. In conclusion, we find no evidence of a main effect of prenatal OP exposure and impaired social responsiveness in our population. However, future investigations within our population will examine whether paraoxonase expression or genetic polymorphisms, modify the above relationships.

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PM2.5 EXPOSURE AND INCIDENT DIABETES AND HYPERTENSION: PRELIMINARY RESULTS FROM THE BLACK WOMEN'S HEALTH STUDY.

*Patricia Coogan, Laura White, Michael Jerrett, Bernardo Beckerman, Jeffrey Yu, Robert Brook, Richard Burnett, Edmund Seto, Lynn Rosenberg (Slone Epidemiology Center, Boston MA 02215)

Laboratory and clinical evidence suggests that fine particulate matter (PM2.5) may contribute to the genesis of chronic conditions like diabetes and hypertension, but there are few epidemiologic data on its relation to incident disease. We assessed the association of exposure to PM2.5 with incident type 2 diabetes (DM) and hypertension (HT) in the Black Women's Health Study (BWHS), a follow-up study of African American women recruited in 1995 and followed biennially with health questionnaires. Participants reported incident DM and HT on questionnaires from 1995-2011. We estimated long-term average PM2.5 levels at participant addresses from 1998-2009 in 56 cities across the U.S. using a hybrid model combining land use regression and Bayesian Maximum Entropy kriging. Mean long-term average PM2.5 levels ranged from 8.8 μg/m3 in Denver to 17.3 μg/m3 in Riverside CA. We used Cox regression models to estimate city-specific hazard ratios (HR) associated with a 1.75 μg/m3 increase in PM2.5, the mean interquartile range in the major cities. City-specific HRs were then pooled in a summary estimate. Of 33,621 women free of DM in 1995, 4078 developed DM over 16 years of follow-up; of 32,638 HT-free women in 1995, 9588 developed HT. After control for age, body mass index, and neighborhood socioeconomic status, the pooled HR for DM was 1.02 (95% CI 0.96-1.08) and for HT it was 0.98 (95% CI 0.95-1.02). These results do not provide evidence of an association between PM2.5 and risk of DM or HT in black women. Future work will assess the effects of traffic-related air pollutants, which were associated with incident DM in previous analyses in BWHS participants living in Los Angeles.

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URINARY BISPHENOL A CONCENTRATIONS AND ENDOMETRIOSIS RISK IN REPRODUCTIVE-AGE WOMEN.

*Kristen Upson, Victoria Holt, Sheela Sathyanarayana, Anneclaire De Roos, Holger Koch, Delia Scholes (Fred Hutchinson Cancer Research Center, Seattle WA 98109)

There is emerging concern about the safety of Bisphenol A (BPA), a chemical used in the production of polycarbonate plastic and epoxy resin. BPA has demonstrated estrogenic actions at environmentally low doses and the majority of the U.S. general population is exposed to this chemical. However, little is known about the possible effects of BPA on endocrine-related disease in reproductive-age women. The purpose of this study was to investigate the relationship between BPA concentrations and risk of a hormonally-mediated disease, endometriosis. We used data from a population-based case-control study of endometriosis conducted among female enrollees, ages 18-49, of Group Health, a large healthcare system in the U.S. Pacific Northwest. Total urinary BPA concentrations were quantified on incident, surgically confirmed endometriosis cases (n = 143) diagnosed between 1996 and 2001 and on population-based controls (n = 287). We estimated odds ratios (OR) and 95% confidence intervals (CI) using unconditional logistic regression, adjusting for urinary creatinine concentrations, age, and reference year. We repeated the analyses restricting the case definition to subcategories of disease which may be etiologically distinct. Our data suggested increased endometriosis risk in relation to total urinary BPA concentrations when comparing third and first quartiles (aOR 1.5, 95% CI: 0.8-3.0) and fourth and first quartiles (aOR 1.5, 95% CI: 0.7-3.1). We observed stronger associations in analyses restricting cases to those with non-ovarian pelvic endometriosis (second vs. first quartile: aOR 3.0, 95% CI: 1.2-7.3, third vs. first quartile: 3.0, 95% CI: 1.1-7.6), a finding not observed for ovarian endometriosis. Assuming the single BPA measurement is representative of exposure during the etiologically relevant time window, our study suggests that BPA may alter the risk of a hormonally-mediated condition among reproductive-age women.

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WATER QUALITY AND ASSOCIATIONS WITH GASTROINTESTINAL CONDITIONS.

*Jyotsna Jagai, Barbara Rosenbaum, Sue Pierson, Lynne Messer, Kristen Rappazzo, Danelle Lobdell (U.S. Environmental Protection Agency, Research Triangle Park NC 27711)

Water quality is quantified using several measures, available from various data sources. These can be combined to create a single index of overall water quality which can be used for health research. We developed a water quality index for all United States counties and assessed associations with gastrointestinal infections (GI) and gastrointestinal symptoms (GS). Data representing water quality were identified. For all counties (n = 3141), variables were constructed and principal components analysis (PCA) used to construct the index. Four categories of rural-urban continuum codes (RUCC1 (most urban) – RUCC4 (most rural)) were used to group counties for multilevel analyses. GI- and GS- (defined per ICD-9CM codes) related hospitalizations (1991-2004) were abstracted from the Center for Medicare and Medicaid Services (CMS), the only comprehensive national hospitalization dataset. Data were aggregated by county of residence; annual hospitalization rates in the elderly (65 + years) per county were calculated. A linear random effects model assessed county-level associations between the water quality index and hospitalization rates. Neither GI (beta coefficient (B): -0.030; 95% Confidence Interval (95% CI): -0.623, 0.563) nor GS (B: -1.558; 95% CI: -6.114, 2.999) hospitalization rates were associated with the water quality index. Low GI case counts and low GS outcome specificity may partially account for the lack of association with overall water quality. Additionally, the elderly may not be the population most at risk for the water quality parameters considered. National level water quality data is limited both spatially and temporally. Though limited, this analysis demonstrates the utility of developing a water quality index for public health research. (This abstract does not necessarily reflect EPA policy.)

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SANITARY SEWER SYSTEMS AND ASSOCIATION WITH GASTROINTESTINAL ILLNESS: A CASE CROSSOVER ANALYSIS OF MASSACHUSETTS DATA, 2006-2008. *Jyotsna Jagai, Genee Smith, Cynthia Lin, Elizabeth Hilborn, Tim Wade, Tim Wade (U.S. Environmental Protection Agency, Research Triangle Park NC 27711)

Sanitary sewer overflows (SSOs) occur when untreated sewage is discharged into water sources before reaching the treatment facility potentially contaminating them with gastrointestinal pathogens. Causes of SSOs include heavy rainfall and rupture/blockage of sewer lines. Few studies have quantified the risk associated with SSO events in the United States. We conducted a case-crossover analysis to assess the association between SSO events and emergency room (ER) visits for gastrointestinal illness (GI). ER visits for GI (n = 370,319) for the years 2006-2008 were obtained from the State of Massachusetts, Division of Health Care Finance and Policy (defined per ICD-9CM codes). SSO events were obtained from the Massachusetts Department of Environmental Protection. A case-crossover analysis was used with each case (ER visit) representing their own control for the city of Lowell, MA. Lowell receives drinking water from the Merrimack River, which is affected by SSO discharges. Two control periods were matched for each case; 21 days before and 21 days after the admission date. Cases and controls were considered exposed if an SSO event occurred within the previous five days and unexposed if there was no SSO event. Data were analyzed using a conditional logistic regression. In Lowell there were 76 documented SSO events and 3,152 ER visits for GI in the time period. For all GI visits there was no association with SSO events: 8.7% of cases and of 9.4% of controls occurred in the three days following an SSO event (Odds Ratio, OR = 0.91, 95% Confidence Interval, 95% CI 0.78-1.06). Among those over 75 years of age there was an elevated but statistically insignificant association (OR = 1.75; 95% CI 0.82-3.72). This analysis demonstrates utility of the case-crossover approach in studying extreme events. Additional analyses will be conducted to evaluate associations in other communities with different water sources. (This abstract does not necessarily reflect EPA policy.)

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SPECIES OF FINE PARTICULATE MATTER AND THE RISK OF PRETERM BIRTH. *Kristen Rappazzo, Julie L Daniels, Lynne C Messer, Charles Poole, Danelle T Lobdell (University of North Carolina - Chapel Hill, NC 27713)

Particulate matter (PM) has been variably associated with preterm birth (PTB), but the roles of PM species have been less studied. We estimated risk of birth in 4 preterm categories (risks reported as PTBs per 106 pregnancies; PTB categories = gestational age of 20-27; 28-31; 32-34; and 35-36) and risk differences (RD(95% confidence intervals)) for PTB categories with change in ambient concentrations of species of PM <2.5 micrometers in aerodynamic diameter: a 0.25 ug/m3 increase in elemental carbon(EC), and 1 ug/m3 increases in organic carbons(OC) nitrates(NO3) and sulfates (SO4). From live birth certificates with clinical estimate of gestation and date of delivery, we constructed a 20-week gestational age cohort of singleton pregnancies between 2000-2005 (n = 1,940,213; 8% PTB (approximately 80,000 per 106 for all categories)). We estimated mean EC, OC, NO3, and SO4 exposures for each week of gestation from monitor-corrected Community Multi-Scale Air Quality modeling data. RDs were estimated using modified Poisson linear regression, adjusted for maternal race, marital status, education, age, and ozone. RD estimates varied by exposure window and outcome period. EC was generally associated with increased risks for births between 28-34 weeks (e.g. a 0.25 ug/m3 increase in EC exposure at gestational week 5 RD = 84(-5, 172) and RD = 97(-50, 243) for birth at weeks 28-31 and 32-34, respectively). OC exposures in late gestation only were positively associated with births between 28-34 weeks. NO3 was not strongly associated with PTB. RDs for SO4 exposure in early and mid gestation were generally positively associated with PTB. Although potential for residual confounding exists, EC and SO4 appear to be influential contributors to of PM2.5's role in PTB. These results indicate diverse periods of action for the species of PM, along with differing windows of vulnerability for the risk of various degrees of PTB. This abstract does not necessarily reflect EPA policy.

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PESTICIDE EXPOSURES IN PAKISTANI FARMERS AND CROPWORKERS. Zaib Hussain, *J Michael Wright (US EPA, Cincinnati OH 45268)

Exposure to pesticides has been associated with adverse health outcomes such as Parkinson's disease (PD). We measured pesticides in 141 cropworkers from five areas of major crop production and pesticide usage in Punjab, Pakistan. Duration and frequency of pesticide use was recorded via questionnaires along with medical history and socio-demographic information, safety precautions and any known pesticide exposure accidents. Complete blood counts and liver function tests (LFTs) and pesticide levels in blood were obtained from 88 respondents during 2 site visits. Pesticide spraying for a one-week duration during the growing season was reported by 32% of study participants Thirty-six percent of participants reported 2-3 weeks of spraying, while 21% reported from 1-4 months of pesticide usage. Thirty-seven participants reported using one pesticide application per treatment, while forty-seven participants used ≥2. Only 13% of participants received pesticide safety training, and 40% of participants were unaware of the name/type of pesticides used. The most commonly reported pesticides were Polytrin C (24%), Karate (19%) and Carbofuran (10%). Pairwise regression results indicated little change in LFTs between the 8-week sampling periods suggesting no demonstrable relationship with pesticide spraying. Preliminary blood data analysis indicated that 7 pesticides (β-hexachlorocyclohexane (β-HCH), Carbofuran, Cartap, Deltamethrin, λ-cyhalothrin, lufenuron and triazophos) were detected in study participants' serum; cartap and β-HCH were the most prevalent. β-HCH is a by-product in the production of the insecticide lindane and other studies have shown elevated β-HCH levels in PD patients. Future analyses will include a case-control study to assess which pesticide components/mixtures are associated with PD. The views expressed in this abstract are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency

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WITHDRAWN

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APPLYING INTEGRATED DOSE-RESPONSE FUNCTIONS TO FUTURE FINE PARTICULATE EXPOSURE IN INDIA. *Vijay Limaye, Wolfgang Schopp, Markus Amann (University of Wisconsin, Madison WI 53726)

Fine particulate matter ($PM_{2.5}$, diameter ≤2.5 μm) is implicated as the most health-damaging air pollutant. Large cohort studies of chronic exposure to $PM_{2.5}$ and mortality risk are largely confined to areas with low to moderate ambient $PM_{2.5}$ concentrations and posit linear dose-response relationships. However, levels of $PM_{2.5}$ in developing countries such as India are typically higher, causing unknown health effects. The 2012 World Health Organization (WHO) Global Burden of Disease posited new, exponential decay dose-response functions for high $PM_{2.5}$ exposure consistent with a biological saturation hypothesis and integrating risk estimates from exposures in ambient air, secondhand smoke, and active smoking. We applied these functions to estimate the cause-specific mortality risk associated with ambient $PM_{2.5}$ exposure in India in 2030 using Greenhouse Gas-Air Pollution Interactions and Synergies (GAINS) model projections. The loss in statistical life expectancy (SLE) was calculated based on risk estimates and baseline national mortality rates. Losses in SLE were aggregated and weighted using national age-adjusted, cause-specific mortality rates. 2030 $PM_{2.5}$ pollution in India reached an annual mean of 74 μg/m^3, nearly eight times the 2005 WHO air quality guideline. The average loss in SLE was 32.5 months (95% Confidence Interval: 29.7-35.2, range: 8.5-42.0), compared to an average of 53.7 months (95% CI: 46.3-61.1) currently estimated in GAINS. Adverse impacts on SLE peaked in Delhi, the most polluted region, and cumulatively 1.1 billion years of life lost were attributed to chronic $PM_{2.5}$ exposure nationwide. These methods likely underestimate the total health burden caused by $PM_{2.5}$ exposure due to model assumptions on minimum age thresholds of pollution effects. The revised dose-response models suggest that the most polluted cities in India will reap major health benefits only with ambitious air pollution mitigation efforts.

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HEAT-RELATED EMERGENCY HOSPITALIZATIONS FOR RESPIRATORY DISEASES IN THE MEDICARE POPULATION. *Brooke Anderson, Francesca Dominici, Yun Wang, Michelle Bell, Meredith McCormack, Roger Peng (Johns Hopkins Bloomberg School of Public Health, Baltimore MD 21205)

Rationale: The heat-related risk of hospitalization for respiratory diseases among the elderly has not been quantified in the United States on a national scale. With climate change predictions of more frequent and more intense heat waves, it is of paramount importance to quantify the health risks related to heat, especially for the most vulnerable. Objective: To estimate the risk of hospitalization for respiratory diseases associated with outdoor heat in the US elderly. Methods: An observational study of ~12.5 million Medicare beneficiaries in 213 United States counties, January 1, 1999 - December 31, 2008. We estimate a national average relative risk of hospitalization for each 10°F (5.6°C) increase in daily outdoor temperature using Bayesian hierarchical models. Measurements and Main Results: We obtained daily county-level rates of Medicare emergency respiratory hospitalizations (ICD-9 464–466, 480–487, 490–492) in 213 United States counties for 1999-2008. Overall, each 10oF increase in daily temperature was associated with a 4.3% increase in same-day emergency hospitalizations for respiratory diseases (95% posterior interval: 3.8, 4.8%). Counties' relative risks were significantly higher in counties with cooler average summer temperatures. Conclusions: We found strong evidence of an association between outdoor heat and respiratory hospitalizations in the largest population of elderly studied to date. Given projections of increasing temperatures from climate change and the increasing global prevalence of chronic pulmonary disease, the relationship between heat and respiratory morbidity is a growing concern.

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ASSOCIATION BETWEEN LYME DISEASE AND WEATHER TYPES IN NEW YORK STATE. *Srishti Shrestha, Wan-Hsiang Hsu, Syni-An Hwang, Scott Sheridan, Shao Lin (New York State Department of Health, Albany NY 12237)

Weather types may affect Lyme disease (LD) incidence via influence on the habitat and lifecycle of the LD vector and pertinent host activities. Prior studies suggest the link between LD and individual meteorological variables; however, association of LD with weather types (WTs) is yet to be explored. We evaluated association of summer LD incidence in New York State (NYS) during 1991-2006 with WTs in the concurrent and preceding seasons. Using the Spatial Synoptic Classification (SSC) system, daily data on six meteorological variables obtained from the National Climatic Data Center were used to classify each day into one of seven WTs: dry polar (DP), dry moderate (DM), dry tropical (DT), moist polar (MP), moist moderate (MM), moist tropical (MT), or transitional (T) for 11 SSC regions in NYS. MapMarker Plus and MapInfo were used to geocode LD data, obtained from NYS Department of Health Communicable Disease Electronic Surveillance System, by patient's ZIP code level address, and to assign SSC WTs to LD cases. Linear regression model with a generalized estimating equation approach to account for correlation within a SSC region was used to estimate the parameter estimate (β) for the association between log summer LD and number of days with certain WT. The results from multivariable models indicated that log summer LD count was positively associated dry moderate WT (β (95% Confidence Intervals):0.07 (0.02, 0.11)) in the preceding summer, adjusting for year, population, and WTs in the model. Significant negative associations of LD with T, MM, MP, and MT WTs, however in different seasons, were also observed; percentage decreases in LD ranged from 6% to 15% per day increase in such WTs. In conclusion, weather types may influence Lyme disease incidence and their associations may be season-specific.

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EXPOSURE TO CADMIUM FROM FOOD AND RISK OF CARDIOVASCULAR DISEASE IN WOMEN - A POPULATION-BASED PROSPECTIVE COHORT STUDY. *Bettina Julin, Charlotte Bergkvist, Alicja Wolk, Agneta Åkesson (Karolinska Institutet, Stockholm Sweden)

Background: The widely spread toxic metal and food-pollutant cadmium is suggested to influence the development of cardiovascular disease (CVD), but to date incidence studies are lacking. Objectives: We evaluated the association between quartiles of food-frequency questionnaire-based estimates of cadmium exposure from food, the dominating source of exposure to the metal, and incident CVD and its subtypes. Methods: From the population-based Swedish Mammography Cohort, 33,333 women were followed prospectively from baseline (1997) through 2010. Relative risks (RRs) with 95% confidence intervals (CIs) were estimated using Cox proportional hazard models. Results: During a mean of 12.2 years of follow-up we identified 3,155 incident cases of total CVD (1,322 cases of myocardial infarction and 1,833 cases of total stroke whereof 1,485 ischemic and 208 hemorrhagic stroke). We observed no association between dietary cadmium exposure and risk of total CVD, myocardial infarction or risk of total stroke or its subtypes. For total CVD, the multivariable-adjusted RR for comparing the highest quartile of cadmium exposure from food with the lowest was 0.96 (95% CI: 0.85, 1.09). The corresponding relative risks were RR 1.07 (95% CI: 0.88, 1.29) for myocardial infarction, RR 0.90 (95% CI: 0.76, 1.05) for total stroke, RR 0.89 (95% CI: 0.74, 1.06) for ischemic stroke and RR 1.11 (95% CI: 0.68, 1.80) for hemorrhagic stroke. We observed a borderline statistically significant increased RR of 1.32 (95% CI: 1.00, 1.75) for myocardial infarction but not for stroke, in the women with the highest dietary and non-dietary exposure (ever smokers). Conclusions: Our study lends no support to an overall association between low-level exposure to cadmium via food and incident CVD.

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FARM RESIDENCE AND LYMPHOHEMATOPOIETIC CANCERS IN A COHORT OF OLDER WOMEN. *Rena Jones, Chu-Ling Yu, John R Nuckols, James R Cerhan, Julie A Ross, Kim Robien, Mary H Ward (National Cancer Institute, Bethesda MD 20892)

Cancer incidence in male farmers has been studied extensively; however, less is known about risk among women residing on farms or in agricultural areas, who may be exposed to pesticides by their proximity to crop fields. We extended a previous follow-up of the Iowa Women's Health Study cohort to further examine farm residence and the incidence of lymphohematopoietic cancers. We investigated crop acreage near homes as surrogates for residential exposure to agricultural pesticides. The cohort of 41,836 Iowa women ages 55-69 years in 1986 reported their residence location (farm, rural, town size based on population) at enrollment. We identified incident cancers (1986-2009) by linkage with the Iowa Cancer Registry. Using a geographic information system, we geocoded addresses and calculated acreage of pasture and row crops within 250, 500, 750, and 1000m of homes using the National Land Cover Database. Cox regression was used to estimate hazard ratios (HR) and 95% confidence intervals (CI). As found in the earlier analysis, risk of acute myeloid leukemia (AML) was significantly higher among women living on farms (HR = 2.15, 95% CI: 1.20-3.85) or in non-farm rural areas (HR = 1.94, 95% CI: 0.89-4.26) compared with women living in towns of >10,000 population. We observed no association between farm or rural residence and non-Hodgkin lymphoma (NHL, overall or for major subtypes) or multiple myeloma. In analyses of crop acreage, we observed no association between crop density and risk of AML, NHL (overall, or for follicular and diffuse large B-cell subtypes) and multiple myeloma. Compared to women with no crops near their homes, acreage of pasture within 500-750m and row crops within 1000m of homes was positively associated with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), but lacked a monotonic trend with tertiles of increasing acreage. These findings suggest that different agricultural exposures may be risk factors for AML and CLL/SLL.

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SERUM POLYCHLORINATED BIPHENYL (PCB) LEVELS AND THEIR ASSOCIATION WITH ENVIRONMENTAL PERCEPTIONS IN ANNISTON, ALABAMA. *C Campagna, D Cibula, P Rosenbaum (SUNY Upstate Medical University, Syracuse, NY 13210)

The relationship between perception of environmental quality and PCB exposures remain poorly understood. A cross-sectional study was conducted in 2005-2007 to study health outcomes, PCB exposure, and environmental perceptions in Anniston, Alabama. Data was collected using the Anniston Community Health Survey (ACHS), with serum PCB levels obtained by blood draw among 774 residents who attended a clinic visit. Descriptive statistics and multifactorial ANOVA were used to assess associations between serum PCB levels (log transformed) and perceptions of environmental quality. Two-tailed results are reported unless noted. Participants were 69% female, 46% African American, with 75% reporting annual household incomes of <$35,000. Twenty percent of residents rated the Anniston environment as excellent, very good, or good, whereas 33% and 26% rated the environment as poor or very poor, respectively. Mean age was 54.8 (SD = 15.9) and mean serum PCB level (sum of 35 PCB congeners in ppb, wet weight), 6.6 (SD = 11.9). Mean PCB levels (ppb) by perception level were: 6.1 (good), 4.5 (fair), 7.7 (poor). After controlling for age, race, and educational attainment, there was a significant effect of environmental perceptions on mean serum PCB levels ($p <. 05$). Planned comparisons revealed a difference in mean PCB levels of participants who reported poor and good environmental perceptions ($p < .05$, one-tailed). Hochberg's GT2 *post hoc* test revealed that mean PCB levels were significantly higher in participants with poor environmental perceptions compared to those with good ($p < .001$) and fair perceptions ($p < .001$). Anniston residents with the poorest environmental perceptions had the highest serum concentrations of PCBs. Funded by the Agency for Toxic Substances and Disease Registry U50/ATU473215. P. Rosenbaum for the Anniston Environmental Health Research Consortium.

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PERSISTENCE OF PROSTATE-SPECIFIC ANTIGEN IN VAGINAL FLUID AFTER EXPOSURE TO SEMEN. *Maurizio Macaluso, Resmi Gupta, Jennifer Collins (Cincinnati Children's Hospital Medical Center, Cincinnati OH 45229)

Prostate-specific antigen (PSA) is an objective marker of unprotected intercourse or condom failure: it is easily detected in vaginal fluid after exposure to semen but its concentration returns to near-zero values within 24-48 hours. It is not clear how long after exposure a sample can be taken with a high likelihood of obtaining a positive result. We reanalyzed data from the first study that evaluated PSA decay after exposure to known amounts of semen. Forty women were exposed to their partner's semen (10 µl, 100 µl and 1000 µl) and took vaginal samples before exposure, immediately after, and at 1, 24 and 48h. PSA was measured by immunoassay. We estimated the rate of PSA decay using mixed models and log-transformed PSA as the dependent variable. Between-subject variation was significant ($p < 0.01$), and random intercepts were retained in the model. The slopes estimating the proportionate rate of decay over time did not significantly differ across subjects but varied according to the initial exposure: PSA levels declined by 12%/h (95% CI: 10-13%) after exposure to 10 µl, by 14%/h (95% CI: 12-16%) after 100 µl and by 20%/h (95% CI: 17-21%) after 1000 µl. We estimated the probability of detecting PSA values above specified thresholds at time points between 1 and 24h: after exposure to 10 µl, the probability of detecting PSA > 1ng/ml declined to 67.5% at 3h, 62.5% at 6h, and 35% at 12h; after 100 µl, the probability of detecting PSA >1ng/ml declined to 74% at 3h, 74% at 6h, and 71% at 12h; after 1000 µl, the probability of detecting PSA >1ng/ml stayed above 95% through 12h, and was also high for PSA >2ng/ml. We conclude that unprotected intercourse can be easily detected from samples collected up to 12h after exposure, whereas the probability of detecting lower-level exposure (as it may occur after condom failure or incorrect use) is high only if samples are collected shortly after exposure.

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MATERNAL MORTALITY AMONG HIV-INFECTED PREGNANT WOMEN IN DAR ES SALAAM, TANZANIA. *Nan Li, Emmanuel Matechi, Donna Spiegelman, Guerino Chalamilla, Ellen Hertzmark, David Sando, Mary Mwanyika Sando, Enju Liu, Aisa Muya, Wafaie Fawzi (Harvard School of Public Health, Boston MA 02115)

Background: In 2010, 56% of the global burden of maternal deaths occurred in Sub-Saharan Africa (SSA). Although maternal mortality declined globally by 3.1% each year since 1990, the decline has been slower in SAA (2.6%) likely because of the HIV epidemic. Methods: Between November 2004 and September 2011, 18,917 women were pregnant at least once after enrolled in the HIV Care and Treatment program in Dar es Salaam, Tanzania. Thirteen percent of these women had multiple pregnancies while in the program. Overall, 21,645 pregnancies occurred. Cox regression models were used to explore the predictors of maternal death. Results: The maternal mortality ratio has been decreasing steadily over the duration of the program. In 2011, it was 658 [95% Confidence Interval (CI): 388-928] per 100,000 live births. In multivariate analysis, older age, earlier year of enrollment, later first visit to HIV clinic after becoming pregnant, elevated alanine aminotransferase, lower CD4 count, and higher WHO HIV stage were independently associated with a greater risk of maternal mortality. Women with mid-upper-arm circumference (MUAC) < 22.0 cm were at a 4-fold higher risk of maternal mortality [Relative Risk (RR): 3.94, 95% CI: 3.04-5.11] than those with MUAC ≥ 22.0 cm. Compared with pregnant women with severe anemia, women with no anemia had a 79% decreased risk of maternal mortality (RR: 0.21, 95% CI: 0.13-0.36). Women who were initiated on antiretroviral therapy (ART) before their pregnancy had a 76% decreased in the risk of maternal mortality (95% CI: 0.16-0.37) than women who were not. The risk of maternal mortality decreased with the length of time on ART during pregnancy, 17% per each additional month (RR: 0.83, 95% CI: 0.79-0.87). Conclusion: Maternal mortality was high among HIV-infected women. Initiating women on ART as early as possible and providing nutritional interventions during pregnancy should be considered as means to reduce the maternal mortality.

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SEXUAL MATURATION IN PERINATALLY HIV-INFECTED AND HIV-EXPOSED YOUTH IN THE ERA OF COMBINATION ANTIRETROVIRAL TREATMENT. *Paige Williams, Mark Abzug, Jiajia Wang, Denise Jacobson, Russell VanDyke, Rohan Hazra, Mitchell Geffner (Harvard School of Public Health, Boston MA 02115)

Background: Perinatally HIV-infected (PHIV) children have historically shown deficient growth and pubertal delay. However, current combination antiretroviral treatment (cART) regimens may help normalize timing of sexual maturation. Methods: We assessed sexual maturation in two large US longitudinal cohort studies conducted 2000-2012. PHIV and HIV-exposed uninfected (HEU) youth had annual Tanner stage assessments. We compared age at sexual maturity (stage 5 for breast (B5) in girls and genitalia (G5) in boys) between PHIV and HEU youth using interval-censored models, adjusting for race/ethnicity and birth cohort. Maturation of pubic hair was also evaluated in boys and girls. Race/ethnicity-adjusted models were used to evaluate early cART initiation (<5 yrs) vs later or no cART. In girls, self-reported age at menarche was compared by HIV status using adjusted Cox regression models. Results: The 2469 PHIV youth (median follow-up = 3.8 yrs) attained sexual maturity significantly later than the 490 HEU youth, with mean ages of 15.4 vs 14.8 yrs at B5 for girls ($p = 0.02$) and 15.9 vs 15.0 yrs at G5 for boys ($p < 0.001$). After adjustment for race/ethnicity and birth cohort, mean delays were attenuated to 4.30 [95% confidence interval (CI):-1.81, 10.40, $p = 0.17$] and 7.74 [95% CI: 1.51, 13.98, $p = 0.015$] months. Age at menarche was significantly later among PHIV than HEU girls (median = 12.5 vs 11.9 yrs, hazard ratio = 0.66 [95% CI: 0.48, 0.92], $p = 0.013$). Among PHIV, lack of early cART was associated with adjusted delays of 3.81 [95% CI:-0.99, 8.62, $p = 0.12$] and 5.14 [95% CI: 0.64, 9.65, $p = 0.025$] months in B5 and G5, respectively. Lack of early cART was associated with significant adjusted delays in pubic hair maturation in both boys and girls. Conclusions: Sexual maturity and menarche occur later in PHIV than in HEU youth. Early initiation of cART in perinatally infected youth, as currently recommended, may result in more normal timing of pubertal maturation.

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SEXUAL BEHAVIORS, STI AND HIV TESTING AND PREVALENCE OF INFECTIONS AMONG MSM IN LATIN AMERICA, SPAIN AND PORTUGAL USING A SOCIAL NETWORKING SITE. *Katie Biello, Joshua Rosenberger, David Novak, Kenneth Mayer, Matthew Mimiaga (The Fenway Institute, Fenway Health, Boston MA 02215)

Background: There is limited data on sexual behaviors, HIV/STI testing and prevalence of infections of men who have sex with men (MSM) across Spanish and Portuguese-speaking countries. Methods: Active members of a popular MSM social networking site in Latin America, Spain and Portugal were invited to participate in an online survey. Frequencies were calculated to describe sexual behaviors, STI and HIV testing practices, and STI and HIV prevalence among 36,477 respondents. Results: Nearly 90% reported having ≥1 sexual partner in the past 3 months (median = 2); 88% had ≥1 male partner, 7% had ≥1 female partner, and 1% had ≥1 transgender partner. Among sexually active respondents, 52% did not always use condoms with male partners; among these 34% had ≥1 male partner of different/unknown HIV serostatus. Additionally, 56% did not always use condoms with female partners; among these, 29% had ≥1 female partner of different/unknown HIV serostatus. Lower rates of unprotected sex were reported among those who had sex with a transgender partner (42%) yet a larger proportion of these men had a transgender partner of a different/unknown HIV serostatus (43%). Ten percent reported paying for and 7% reported getting paid for sex in the past year. Fourteen percent reported being diagnosed with an STI in the past year, and 46% reported not being tested for STIs in that period. Self-reported HIV prevalence was 9% and 33% reported not being tested for HIV at least yearly. Unprotected sex and serodiscordant unprotected sex were associated with having a diagnosed STIs in the past year and a prevalent HIV infection ($p < .05$). Conclusion: Among MSM using a social networking site across Latin America, Spain and Portugal, rates of STI and HIV testing were suboptimal and rates of unprotected and HIV serodiscordant unprotected sex were high across gender of partners and region. Results are consistent with data from other large cohorts of men recruited online.

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SEX DIFFERENCES IN RESPONSES TO ANTIRETROVIRAL TREATMENT IN SOUTH AFRICAN HIV-INFECTED CHILDREN ON RITONAVIR-BOOSTED LOPINAVIR-BASED AND NEVIRAPINE-BASED TREATMENT. *Stephanie Shiau, Stephen Arpadi, Renate Strehlau, Leigh Martens, Faeezah Patel, Ashraf Coovadia, Elaine J Abrams, Louise Kuhn (Columbia University, New York NY 10032)

Background: Evidence in HIV-infected adults shows higher rates of antiretroviral treatment (ART) complications in women compared to men. However, few studies have assessed sex differences in children. Here we investigate if there are differences in responses to two ART regimens between young HIV-infected boys and girls. Methods: This secondary analysis compares ART outcomes in HIV-infected boys and girls who initiated ritonavir-boosted lopinavir (LPV/r)-based ART before 24 months of age in Johannesburg, South Africa from 2005-2007 and were randomized to remain on LPV/r or switch to nevirapine (NVP)-based ART. HIV-1 viral load (VL), CD4 count, total cholesterol (TC), HDL, LDL, triglycerides, and anthropometrics were measured at regular follow up visits. Outcomes were compared between sexes within treatment strata as well as between treatment groups within sex strata. Results: A total of 323 children (median age 8.8 months, IQR 5.1-13.5) including 168 boys and 155 girls were initiated on LPV/r-based ART. 195 children were randomized and 156 children completed long-term follow up. No sex differences in virological failure (confirmed VL > 1000 copies/mL) by 156 weeks post randomization were observed within treatment groups. Girls who switched to NVP had a significantly greater mean CD4 response than boys switched to NVP as well as compared to girls continuing on LPV/r at 24, 64, and 100 weeks post randomization. Upon exit from the study, girls on LPV/r had a higher TC:HDL ratio and lower mean HDL concentration than boys on LPV/r, as well as compared to girls switched to NVP. Conclusions: Immunologic response to ART was strongest for girls who switched to NVP. Sex differences were also noted in lipid profiles, with a less favorable outcome for girls who remained on LPV/r. Future studies are warranted to determine the biological mechanisms and clinical significance of these differences.

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CHANGING TREND IN ADHERENCE TO HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) IN THE MULTICENTER AIDS COHORT STUDY. *Shilpa Viswanathan, Roger Detels, Bernard J. C Macatangay, Lisa P Jacobson (Johns Hopkins Bloomberg School of Public Health, Baltimore MD 21205)

Background: Adherence to HAART has been a barrier for universal administration at early stages of HIV infection. Over time, formulations of HAART became simpler to use and their pharmacokinetics have improved. Goal: To describe trends in adherence to HAART between 2001 and 2011, and determine if >95% adherence is currently needed for HIV RNA suppression. Methods: Serial cross-sectional and longitudinal analyses were nested in the Multicenter AIDS Cohort Study, a large cohort study of HIV in men who have sex with men (MSM). Adherence was calculated using an established algorithm based on reported use over the 4 days prior to the 6 month study visit. The adherence percent and proportion with suppressed HIV RNA were graphically depicted, and piecewise linear regression was used to test if the observed change in the proportion suppressing HIV RNA among those with <90% adherence over time was significant. Results: Among the 1,245 HAART users seen at least once since 2000, those reporting 100% adherence increased from 81% in 2001 to 90% in 2011. Restricting the sample to those who were active since 2009 (N = 1,045) to avoid drop-out bias, this trend persisted. Among those with <90% adherence, the proportion suppressing HIV RNA also increased since 2001 from 50% to 88% in 2006 ($P < 0.05$) and has remained relatively constant between 80% and 85% since 2006 when a single pill regimen (Atripla) became available. A measure of over- reporting bias is the proportion of 100% adherers with detectable HIV RNA. Since 2001, this decreased from 32% to 10%. Conclusion: The observed improvement in reported adherence in this cohort of MSM is consistent with easier drug formulations. The high proportion reporting 100% adherence limits the generalizability to other risk groups. Although perfect adherence is optimal, the high proportion suppressing virus, even among those with <90% adherence, suggests that current HAART may be more universally prescribed.

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SELECTION OF OPTIMAL PHARMACY REFILL-BASED MEASUREMENTS TO MONITOR ANTIRETROVIRAL ADHERENCE.

*Cassidy Henegar, Daniel Westreich, Mhairi Maskew, M Alan Brookhart, Annelies Van Rie (University of North Carolina, Chapel Hill NC 27599)

Adherence to highly active antiretroviral therapy (HAART) is key to achieving and maintaining viral suppression in HIV-infected individuals. Routinely collected pharmacy data are convenient and inexpensive means to assess HAART compliance, and numerous adherence indicators have been derived from such data. The comparative utility of these measures, however, has not been assessed systematically. We used HAART prescription refill data from 29,937 pharmacy visits made by 11,085 adult HIV-positive patients at the Themba Lethu Clinic in Johannesburg, South Africa, to assess the ability of several adherence indicators to predict virologic failure. Using logistic regression with generalized estimating equations, we compared the magnitudes of the odds ratios for each indicator. Concordance statistics were used to assess the discriminative ability of individual models. Two simple binary indicators for adherence, "attending late" vs. "attending clinic by scheduled visit date" (Odds Ratio (OR): 1.27, 95% Confidence Interval (CI): 1.16, 1.38) and "running out of pills" vs. "complete pill coverage between visits" (OR: 1.26, 95% CI: 1.15, 1.39), were able to distinguish between adherent and non-adherent behavior patterns as well as more complicated indicators calculated from the same pharmacy data. All adherence measures were more strongly associated with virologic failure among patients scheduled to refill their prescriptions every two months compared to those with monthly refills, including the "late" vs. "attending by scheduled date" indicator (OR for bimonthly refills: 1.22, 95% CI: 1.09, 1.39; OR for monthly refills: 0.99, 95% CI: 0.84, 1.15). Our results suggest that simple binary indicators of adherence based on pharmacy refill data predict virologic outcomes and could serve as routine indicators of adherence in resource limited settings.

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HUMAN PAPILLOMAVIRUS (HPV) AND HPV VACCINE AWARENESS AMONG U.S. AND INTERNATIONAL STUDENTS AT A MID-WESTERN UNIVERSITY.

*Sameer Gopalani, Madhav Bhatta (Kent State University, Kent OH 44240)

Although two 3-dose human papillomavirus (HPV) vaccines are available for females and one for males to protect against HPV-related diseases including cervical cancer, uptake of HPV vaccines remains very low globally. The purpose of this study was to assess the level of awareness and knowledge about HPV and HPV vaccines among U.S. (citizens or permanent residents) and international students at a mid-western university. A cross-sectional study was conducted among a random sample of 502 undergraduate and graduate students at a large public university. An anonymous and self-administered online and paper-based survey was used to assess socio-demographics, knowledge about HPV and HPV vaccines, and HPV vaccine beliefs, acceptance, and uptake. Multivariable logistic regression analysis was performed to assess the relationship between student characteristics and lack of HPV and HPV vaccine awareness. Of the 502 participants, 27.7% were international students primarily from Asia, 24.2% were male, 82.8% were single, and the median age was 23.0 years. Overall, 15.0% and 15.4% respectively reported not being aware of HPV and HPV vaccines. International (Odds Ratio; 95% confidence interval: 19.0; 9.6, 37.8), 21-23 year old (2.4; 1.01, 5.5) and male (2.3; 1.3, 4.3) students were significantly more likely to be not aware of HPV than domestic, 20 years or younger and female students. Similarly, international (18.2; 9.6, 35.9) and male (2.2; 1.2, 4.1) students were significantly more likely to be not aware of HPV vaccine than domestic and female students. Lower HPV and HPV vaccine awareness among international students is an indicator of the awareness level in their home countries, where the burden of cervical cancer is most likely to be higher than the U.S. Increasing HPV and HPV vaccine globally is the first step toward global cervical cancer prevention efforts.

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THE CHALLENGE OF CONCURRENCY AS A MEASURE IN NETWORKS CHARACTERIZED BY SHORT INTERVALS BETWEEN MULTIPLE PARTNERS: PATTERNS OF PARTNERING AMONG MEN WHO HAVE SEX WITH MEN IN SHANGHAI, CHINA.

Sarah Jane Steele, Lynne Messer, Peter Leone, William Miller (University of North Carolina Gillings School of Global Public Health, Chapel Hill NC 27516)

The Centers for Disease Control recommends routine HIV testing in clinical settings. The evidence for an increase in HIV diagnoses as a result of these testing programs is inconclusive. We examined the North Carolina (NC) expanded HIV testing program's impact on HIV testing and the diagnosis of new HIV-positive cases in sexually-transmitted disease (STD) clinics. The NC expanded HIV testing program implemented routine, opt-out HIV testing in STD clinics in November 2007. All persons aged 18-65 who were tested for HIV in NC STD clinics July 2005-June 2011 were analyzed. The monthly change in the number of HIV tests performed, number of new HIV-positive cases identified, and HIV positivity proportion per 1000 tests before and after the intervention were evaluated. Interrupted time series analysis with autoregressive components was used to account for underlying temporal trends and autocorrelation. From July 2005-June 2011, 414,612 HIV tests were performed, yielding 1293 new HIV cases (0.3%). Prior to the intervention, the number of HIV tests performed increased by 60 tests per month (rate difference [RD] = 60.4, 95% confidence interval [CI]: 50.6, 70.2). However, after the intervention, the monthly increase in testing slowed to 42 tests per month (RD = 41.7, 95% CI: 36.8, 46.6). After the introduction of the intervention, neither the number of new HIV-positive cases identified nor the HIV positivity per month differed from expected case detection trends without the intervention (number of new HIV-positive cases: RD = -0.11, 95% CI: -0.33, 0.11; HIV positivity per 1000 tests: RD = 0.036, 95% CI: -0.001, 0.073). Despite the introduction of an expanded HIV testing program in NC STD clinics, no change in HIV testing or HIV case detection was observed. A lack of evidence for program yield in a clinical setting with high baseline levels of HIV testing questions the intervention's appropriateness.

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EXPANDED HIV TESTING PROGRAM IN STD CLINICS FAILS TO IMPACT DIAGNOSIS OF NEW HIV-POSITIVE CASES.

*Pamela Klein, Lynne Messer, Peter Leone, William Miller (University of North Carolina Gillings School of Global Public Health, Chapel Hill NC 27516)

The Centers for Disease Control recommends routine HIV testing in clinical settings. The evidence for an increase in HIV diagnoses as a result of these testing programs is inconclusive. We examined the North Carolina (NC) expanded HIV testing program's impact on HIV testing and the diagnosis of new HIV-positive cases in sexually-transmitted disease (STD) clinics. The NC expanded HIV testing program implemented routine, opt-out HIV testing in STD clinics in November 2007. All persons aged 18-65 who were tested for HIV in NC STD clinics July 2005-June 2011 were analyzed. The monthly change in the number of HIV tests performed, number of new HIV-positive cases identified, and HIV positivity proportion per 1000 tests before and after the intervention were evaluated. Interrupted time series analysis with autoregressive components was used to account for underlying temporal trends and autocorrelation. From July 2005-June 2011, 414,612 HIV tests were performed, yielding 1293 new HIV cases (0.3%). Prior to the intervention, the number of HIV tests performed increased by 60 tests per month (rate difference [RD] = 60.4, 95% confidence interval [CI]: 50.6, 70.2). However, after the intervention, the monthly increase in testing slowed to 42 tests per month (RD = 41.7, 95% CI: 36.8, 46.6). After the introduction of the intervention, neither the number of new HIV-positive cases identified nor the HIV positivity per month differed from expected case detection trends without the intervention (number of new HIV-positive cases: RD = -0.11, 95% CI: -0.33, 0.11; HIV positivity per 1000 tests: RD = 0.036, 95% CI: -0.001, 0.073). Despite the introduction of an expanded HIV testing program in NC STD clinics, no change in HIV testing or HIV case detection was observed. A lack of evidence for program yield in a clinical setting with high baseline levels of HIV testing questions the intervention's appropriateness.

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USING HIV SURVEILLANCE DATA TO IDENTIFY AREAS FOR TARGETED HIV CONTROL STRATEGIES. *Christina Schumacher, Ravikiran Muuva, Carolyn Nganga-Good, Rafiq Miazad, Jacky Jennings (Johns Hopkins School of Medicine, Baltimore MD 21224)

The limited effectiveness of previous efforts and dramatic reductions in funds for HIV/AIDS prevention and care programs, argues for a shift of public health resources for HIV from prevention activities to targeted control strategies. Targeted control strategies seek to limit transmission, i.e. the transmission of HIV from an infected individual to an uninfected individual. To implement targeted HIV control in Baltimore, Maryland, we sought to create a tool to distinguish geographic areas of No (NT), Low (LT), and High (HT) transmission, and to determine the stability of these classifications over time. Using HIV surveillance data routinely collected by the Baltimore City Health Department (BCHD), we geocoded residential addresses of all persons newly diagnosed with HIV from 2009 to 2011 and aggregated the cases to census tracts (CT). CTs were classified as NT (0 diagnoses), LT (50th to 75th percentile), and HT (>75th percentile) using all three years of data (i.e. pooled data) and separately, for each year. We used a weighted Kappa statistic (K) to assess agreement of transmission area classified using 1) the pooled vs. annual data; and 2) the annual data on a one-year lag (2010 vs. 2009 and 2011 vs. 2010). Overall, 93% of the 815 HIV diagnoses reported to BCHD from 2009 to 2011 had a geocodable address; 83% (165/200) of CTs had at least 1 new HIV diagnosis (range: 0-21). Of these, 58% and 24% were classified as LT and HT, respectively. Substantially fewer CTs were classified as HT in 2009 (18.5%), 2010 (17.0%), and 2011 (16%) than in the pooled data. Overall agreement between the classifications with the pooled data was fair to good (2009: $K = 0.61$; 2010: $K = 0.45$; 2011: $K = 0.49$). However, agreement was slight between 2009-2010 ($K = 0.35$) and 2010-2011 ($K = 0.25$). Our transmission area definitions may be limited due to small numbers of diagnoses per CT and are, therefore, unstable. Better tools are needed to identify areas for targeted HIV control.

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EVALUATING THE IMPLEMENTATION OF HIV-EXPOSED INFANT CARE: OUTCOMES FROM A FAMILY-CENTERED HIV PREVENTION, CARE, AND TREATMENT PROGRAM IN KINSHASA, DEMOCRATIC REPUBLIC OF CONGO. *Lydia Feinstein, Andrew Edmonds, Jean Lambert Chalachala, Vitus Okito, Jean Lusiama, Annelies Van Rie, Benjamin Chi, Stephen R Cole, Frieda Behets (The University of North Carolina at Chapel Hill, Department of Epidemiology, Chapel Hill NC 27599)

To assess implementation of HIV-exposed infant care in Kinshasa, Democratic Republic of Congo, we conducted a cohort study of 1690 infants enrolled between August 2008 and July 2012 at two HIV care and treatment sites. Accounting for competing risks, we estimated the cumulative incidences of receiving an HIV virologic test, loss to follow-up (LTFU), HIV infection, and death by age 18 months, as well as combination antiretroviral therapy (cART) initiation by HIV-infected infants by age 24 months. We compared outcomes between two periods (before and after August 2010) with time in care as the timescale. Median enrollment age was 21 days (interquartile range [IQR]:15-76) before August 2010 and 19 days (IQR:15-49) thereafter. Overall, 70% of infants received a prevention of mother-to-child transmission regimen; mothers received cART (39%) or another regimen (52%). The proportions of infants and mothers who failed to receive a regimen declined after August 2010, from 43% to 18% and 15% to 5%, respectively. The cumulative incidence (95% confidence interval [CI]) of having an HIV test was 0.78 (0.75,0.81) before August 2010 and 0.93 (0.91,0.95) thereafter. The median (IQR) time between enrollment and testing decreased from 52 (29-309) days in period 1 to 29 (5-36) days in period 2. Overall, 150 infants became infected with HIV, 68 died and 240 were LTFU. Before August 2010, the cumulative incidences (95% CI) of HIV, death, and LTFU were 0.34 (0.05,0.67), 0.07 (0.05,0.10) and 0.22 (0.16,0.28), respectively, and after August 2010 the estimates were 0.07 (0.05,0.09), 0.03 (0.02,0.04) and 0.16 (0.13,0.19). Among HIV-infected infants, the cumulative incidence (95% CI) of starting ART was 0.78 (0.67,0.85) before August 2010 and 0.95 (0.81,0.99) thereafter; the median (IQR) time from enrollment to ART was 164 (84-477) days in period 1 and 101 (38-197) days in period 2. Implementation of HIV-exposed infant care in Kinshasa is challenging but has improved over time.

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ONLINE SEROSORTING BEHAVIORS AND HIV DISCLOSURE AMONG MEN WHO HAVE SEX WITH MEN. *Michael LeVasseur, Seth Welles (Drexel University School of Public Health, Philadelphia PA 19102)

Background: Men who have sex with men (MSM) remain at increased risk for HIV. Recent studies report that more than 50% of MSM who seek partners online engage in unprotected anal intercourse (UAI). Some researchers have suggested that this increase has been accompanied by seroadaptive behaviors, such as serosorting (intercourse with seroconcordant partners) to reduce the risk of HIV transmission. This research explores the association between the desire to serosort and disclosure of HIV status in an Internet sample of MSM. Methods: 1,001 MSM were recruited online between April and December 2005 to participate in an online survey. Internet usage habits, sexual behaviors, HIV disclosure, and beliefs about serosorting were evaluated in a subsample of men who reported having had sex with an online male partner. Descriptive and regression analysis was used to explore the association between serosorting and HIV disclosure. Results: Of 464 MSM included in our subsample, 86.9% reported having disclosed their HIV status with their last online sex partner and 74.8% expressed a desire to serosort. Those who reported a desire to serosort had 3.99-times the odds of HIV disclosure than those who did not report the desire ($p = 0.012$). Those who discussed condom use or non-use had 4.5-times the odds of disclosing their status than those who did not discuss condoms ($p = 0.03$). In contrast, HIV+ men had a 92% reduction in the odds of disclosure ($p < 0.001$) compared to those who are not and had more than 6-times the odds of unprotected anal intercourse with the last partner they met online ($p < 0.001$). Conclusions: While, MSM who desire partners of the same serostatus or discuss condom use are more likely to disclose their HIV status than those who do not, those who are HIV+ do not disclose their HIV status to their Internet partners. Since HIV+ men are more likely to report UAI efforts should be made to increase HIV disclosure of HIV+ MSM who use the Internet to find sex partners.

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INFLAMMATION IS ASSOCIATED WITH SEPARATE DOMAINS OF COGNITIVE DECLINE IN THE ELDERLY. *Gloria C Chi, Annette L Fitzpatrick, Monisha Sharma, Nancy S Jenny, Oscar L Lopez, Steven T DeKosky (University of Washington, Seattle WA 98195)

There is evidence that cardiovascular factors influence cognitive decline and dementia, and inflammation may be an important contributor to these conditions. We investigated whether four inflammatory biomarkers: endothelin-1 (ET-1), pentraxin 3 (PTX3), serum amyloid protein (SAP), and receptor for advanced glycation endproduct (RAGE) were associated with decline in five domains of cognition in an elderly population. Community-dwelling older adults from the Ginkgo Evaluation of Memory Study ($n = 1,157$, age 75+) free of dementia at baseline were followed over 7 years. Blood biomarker levels were measured at baseline and neuropsychological tests were administered at baseline and repeated yearly after the 5th year of follow-up. Specific domains of cognition were evaluated as follows: California Verbal Learning Test long delayed recall to assess memory, Block Design for construction, Word Generation for language, Trail Making Test A for psychomotor speed, and Trail Making Test A and B to assess executive function. Generalized estimating equations were used, adjusting for demographics and cardiovascular risk factors. ET-1 was found to be negatively associated with memory ($p = 0.03$), and language ($p = 0.004$). Further adjustment for the APOE-ε4 genotype attenuated these effects. PTX3 was negatively associated with construction ($p = 0.03$) and positively associated with psychomotor speed ($p = 0.007$). SAP was positively associated with memory ($p = 0.04$) and further adjustment for APOE-ε4 attenuated this association. RAGE was not associated with any cognitive domains. Our results suggest that inflammation plays a role in cognitive decline but that these relationships may be complex. Further research is needed to understand their role in early detection of dementia.

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OBESITY DURING CHILDHOOD AND ADOLESCENCE INCREASES SUSCEPTIBILITY TO MULTIPLE SCLEROSIS AND IS INDEPENDENT OF ESTABLISHED GENETIC AND ENVIRONMENTAL RISK FACTORS.

*Milena Gianfrancesco, Brigid Acuna, Ling Shen, Farren Briggs, Hong Quach, Allan Bernstein, Anna Hedstrom, Ingrid Kockum, Lars Alfredsson, Tomas Olsson, Cathy Schaefer, Lisa Barcellos (UC Berkeley School of Public Health, Berkeley CA 94720)

Objective: To investigate the association between obesity and multiple sclerosis (MS) while accounting for established genetic and environmental risk factors. A total of 3,455 individuals were studied. Methods: Participants were female members of Kaiser Permanente Medical Care Plan, Northern California Region (KPNC) (985 MS cases and 588 controls). Logistic regression models were used to estimate odds ratios (ORs) with 95% confidence intervals (95% CI). Body mass index (BMI)/size was the primary predictor of each model, adjusted for age, cigarette smoking and college education. KPNC data were combined with Swedish data (831 MS cases and 1,051 controls) to further examine the association between BMI at age 20 and MS in a meta-analysis. Results: Report of being a little/very overweight at age 10 and at age 20 were significantly associated with MS ($p = 3.5 \times 10^{-3}$ and 1.8×10^{-3}, respectively). Having a BMI greater than or equal to 30 kg/m2 during one's 20's was associated with 2.08 increased odds of MS (95% CI 1.14, 3.82; p = 0.017). Multivariate models demonstrated a consistent independent association after controlling for history of infectious mononucleosis and genetic risk factors, including HLA-DRB1*15:01 and established non-HLA MS alleles. A meta-analysis of over 3,000 females confirmed a twofold risk of MS for BMI greater than or equal to 30 kg/m2 (OR = 2.01, 95% CI 1.34, 3.02; $p = 6.8 \times 10^{-4}$) and a significant trend across categories (3.8×10^{-6}). Interpretation: Being overweight during childhood and adolescence are shown for the first time to be associated with MS in females independent of well-established genetic and environmental factors. Body mass represents a modifiable factor that could potentially decrease risk associated with developing MS.

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CREUTZFELDT-JAKOB DISEASE AMONG AMERICAN INDIANS AND ALASKA NATIVES IN THE UNITED STATES, 1983-2009.

*Robert Holman, Ryan Maddox, Arianne Folkema, Arialdi Minino, Ermias Belay, Lawrence Schonberger (Centers for Disease Control and Prevention, Atlanta GA 30333)

Background/Introduction: Creutzfeldt-Jakob disease (CJD) occurrence among American Indians and Alaska Natives (AI/ANs) is of special interest, in part because of the high prevalence of hunting and venison consumption in this population. Such behaviors could place AI/ANs at increased risk of prion disease if chronic wasting disease (CWD) were found to transmit to humans. Materials/Methods: Death records with CJD as any-listed cause of death for US residents identified from the national multiple cause-of-death data and other surveillance mechanisms for 1983 through 2009 were analyzed, and incidence was calculated by race. Available death certificates and medical records were collected and examined for AI/AN decedents. Results: During 1983 through 2009, 15 decedents with CJD as a cause of death were reported as AI/AN race. The average annual age-adjusted CJD incidence for AI/ANs was 0.39 per 1,000,000 persons. The rate for whites (1.07) was higher compared to that for AI/ANs (RR = 2.9, 95% CI = 1.8-4.9) and blacks were similar (0.41; RR = 1.1, 95% CI = 0.7-1.9). The median age at death was 65 years (range 39-85 years), similar to those for whites and blacks (68 and 66 years, respectively); four (27%) AI/AN decedents were younger than 55 years of age. Most of the AI/AN decedents were males (60%). Decedents were reported from 13 states; none resided in the states with the longest known presence of CWD, Colorado, Wyoming, and Nebraska. Conclusion: The reported CJD incidence for AI/ANs appears lower than that for whites and similar to that for blacks, although the CJD incidence for AI/ANs is likely underestimated due to racial misclassification of AI/ANs. Continued monitoring of CJD occurrence in this population is important as CWD spreads into new areas.

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THE EPIDEMIOLOGICAL BURDEN OF LOWER LIMB SPASTICITY IN ADULTS: A SYSTEMATIC REVIEW.

Alison Martin, Seye Abogunrin, *Jerome Dinet, Hannah Kurth (IPSEN, Boulogne Billancourt France)

Lower limb spasticity (LLS) is a recognised feature and sequelae of various diseases, but little is known about the international scale of the problem. We therefore conducted a systematic review of MEDLINE, EMBASE and grey literature sites, for evidence on the epidemiological burden of LLS in adults, and thereby identified and assessed 22 relevant studies published between 2002 and 2012. The studies suggested that LLS occurs in 29-37% of stroke patients, 44-69% of patients with multiple sclerosis (MS), 75% of adults with cerebral palsy (CP), 13% of patients with traumatic brain injury, and 92% of patients with primary lateral sclerosis. The severity of spasticity varied according to the underlying pathology, with, for example, nearly 95% of stroke patients having mild LLS, but more severe symptoms occurring in patients with MS and CP. The prevalence of LLS varied between countries overall, but was relatively consistent within each underlying-disease group, regardless of geographic location. Early impairment of daily functioning, early leg weakness, and a history of smoking are possible risk factors for development of LLS after a stroke, but evidence on predisposing factors was otherwise sparse. The data also suggested that LLS may increase the likelihood of deep vein thrombosis after stroke by as much as 28-fold. However, we found no clear association between LLS and occurrence of pain, development of contractures, or risk of falls. The review identified gaps in the research on the epidemiological burden of LLS, which is surprising given the condition's high prevalence among people with common disorders, such as stroke. The dearth of high-quality evidence for LLS suggests a lack of both awareness and interest in this widespread clinical problem.

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THE RELATIONSHIP BETWEEN DEPRESSIVE SYMPTOMS AND THE INCIDENCE OF DEMENTIA IN A POPULATION-BASED SAMPLE OF OLDER MEXICAN AMERICANS.

*Joanne M Penko, John Neuhaus, Mary N Haan (University of California, San Francisco, San Francisco CA 94107)

No studies have evaluated the association between depressive symptoms and the risk of dementia among older Mexican Americans. Few have analyzed depressive symptoms as a time-varying (TD) predictor. We evaluated the relationship between depressive symptoms and incident dementia over 10 years among participants in the Sacramento Area Latino Study on Aging, a population based cohort of Mexican Americans 60 years or older in 1998. A total of n = 1534 were free of dementia at baseline and had non-missing data. Depressive symptoms were evaluated using the Center for Epidemiological Studies Depression Scale (CES-D). Dementia diagnosis was based on standard diagnostic criteria. We used Cox proportional hazard models to produce adjusted hazard ratios and 95% confidence intervals. We modeled CES-D score at baseline and, in separate models, as a TD predictor. Final models were adjusted for age, education, sex, waist circumference, smoking, alcohol consumption, hypertension, cardiovascular disease and diabetes. The sample had a mean age of 70.1 years at baseline, 58.6% were women, and 68.8% had less than a high school education. At baseline, one-fourth (25.0%) reported elevated depressive symptoms (EDS) (CES-D score greater than 15). Those who reported EDS compared to those who did not had a 62% increased hazard of dementia in fully adjusted models (aHR = 1.62, 95% CI = (1.04, 2.53)). When CES-scores were modeled as a TD predictor with a one-year lag, those with EDS had an 80% increased hazard of dementia (aHR = 1.80, 95% CI = (1.24, 2.61)). Though we identified a stronger association between EDS and dementia when depressive symptoms were measured proximal to dementia diagnosis, the association was not substantially increased. The proportion of people reporting EDS was higher compared to samples from prior studies, indicating that depressive symptoms may represent an important prodromal feature of dementia among Mexican Americans.

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CHARACTERISTICS OF U.S. ADULTS WHO FALL FREQUENTLY: THE BALANCE AND DIZZINESS SUPPLEMENT TO THE 2008 NATIONAL HEALTH INTERVIEW SURVEY (NHIS). *Howard J Hoffman, Chuan-Ming Li, Katalin G Losonczy, Daniel A Sklare, Helen S Cohen, Charley C Della Santina (National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Bethesda MD 20892)

The 2008 NHIS Balance and Dizziness Supplement is the first nationally representative survey of non-institutionalized adults (18+ years) to include extensive coverage of disturbances in balance function. Respondents (N = 21,782) were asked about dizziness/imbalance (DI) symptoms during the past year; symptom severity and timing; provoking and palliating factors; use of balance aids; physical and psychological problems; medicine and drug use; conditions associated with episodes; health care utilization; diagnoses and use of treatments; outcomes; limitations of activities; days of school or work missed; numbers of falls in the past 1 and 5 years; and injury from falling. The prevalence of DI in the past year was 14.8% (33.4 million adults); higher for women, 18.3%, than men, 11.1%. Characteristics of frequent fallers (FF) who reported falling at least once a month during the past year were compared to those that fell less (FL) often and those that did not fall (NF). The FF prevalence was 1.3%, FL 10.1%, and NF 88.6%. Falling risk (FF + FL) increased for older adults (65+ years), odds ratio (OR) = 1.48, 95% confidence interval (CI): 1.31-1.68; women, OR = 1.37, CI: 1.24-1.53; non-Hispanic whites, OR = 1.56, CI: 1.39-1.76. FF were more likely to report DI symptoms, OR = 10.90, CI: 7.78-15.28. Respondents with DI accounted for 64.1% of FF but aging, female sex, and race did not increase their falling risk. Unsteadiness (28.0%) was the most bothersome DI symptom, next were lightheadedness (18.4%) and fainting (16.3%). Among those with DI, 33.3% of FF described their symptoms as a big or very big problem, compared to 12.4% for FL and 7.2% for NF. Injuries from falling were reported by 46.9% of FF and 37.9% of FL. More than half (51.9%) of FF with DI symptoms reported health conditions as reasons for falling. These analyses show that DI symptoms during the past year are common, disabling, and costly, conferring greatly increased risk for frequent and injurious falls.

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MILK CONSUMPTION AND CARDIOVASCULAR RISK FACTORS IN OLDER CHINESE: THE GUANGZHOU BIOBANK COHORT STUDY. *Yangbo Sun, Chaoqiang Jiang, Kar Keung Cheng, Weisen Zhang, Gabriel M Leung, Tai Hing Lam, C Mary Schooling (The University of Hong Kong, Hong Kong SAR China)

Background: Dairy products consumption is increasingly common globally. Most of the evidence concerning dairy products comes from observational studies in western populations which are inevitably open to confounding. To triangulate the evidence concerning dairy products, we examined the association of whole cow's milk consumption with cardiovascular risk factors in a non-Western setting with a different pattern of milk consumption and cardiovascular diseases from Western populations. Methods: We used multivariable censored linear or logistic regression to examine cross-sectionally the adjusted associations of whole cow's milk consumption (none (n = 14892), 1-3/week (n = 2689) and 3 + /week (n = 2754)) with cardiovascular risk factors in older Chinese (≥50 years) in the Guangzhou Biobank Cohort Study. Results: Whole cow's milk consumption was negatively associated with systolic blood pressure (3 + /week compared to none -2.56 mmHg, 95% confidence interval (CI) -3.63 to -1.49), diastolic blood pressure (-1.32 mmHg, 95% CI -1.87 to -0.77) and triglycerides (-0.057 mmol/L, 95% CI -0.11 to -0.002), but was positively associated with HDL-cholesterol (0.023 mmol/L, 95% CI 0.006 to 0.04) and fasting plasma glucose (0.08 mmol/L, 95% CI 0.006 to 0.16) adjusted for age, sex, phase of study, socio-economic position, lifestyle (smoking, alcohol use and physical activity) and adiposity, but had no obvious association with LDL-cholesterol or the presence of diabetes. Conclusions: Whole cow's milk consumption had heterogeneous associations with cardiovascular risk factors, potentially suggesting that whole cow's milk influences cardiovascular risk factors by risk factor specific biological pathways which have different effects on blood pressure and lipids than on fasting glucose.

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PLASMA VITAMIN D BIOMARKERS AND LEUKOCYTE TELOMERE LENGTH. *Jason Liu, Jennifer Prescott, Edward Giovannucci, Susan Hankinson, Bernard Rosner, Jiali Han, Immaculata De Vivo (Department of Epidemiology, Harvard School of Public Health, Boston MA 02115)

Background: Vitamin D may reduce telomere shortening through anti-inflammatory and anti-cell proliferation mechanisms, and this study examines the association between vitamin D and relative leukocyte telomere length by using both plasma 25-hydroxyvitamin D [25(OH)D] and 1,25-dihydroxyvitamin D [1,25(OH)2D] biomarkers. Methods: Vitamin D biomarker levels and leukocyte telomere length were measured using plasma samples collected in 1989-1990 from participants of the Nurses' Health Study (NHS), a study of nurses from 11 U.S. states. 1,424 participants were measured for 25(OH)D and 837 for 1,25(OH)2D. Genotyping was performed on 480 participants with a telomere measurement on 12 single nucleotide polymorphisms (SNPs) in vitamin D-related genes. Linear and logistic regression models were used. Results: Higher 25(OH)D was significantly associated with longer telomere length (P-trend = 0.05), and the odds ratio (OR) increased from 1.07 (P = 0.65) when comparing the second lowest quartile of 25(OH)D with the lowest, to 1.59 (P = 0.01) when comparing the highest quartile with the lowest. 1,25(OH)2D and the vitamin D-related SNPs were not significantly associated with telomere length. Total calcium intake significantly modified the association between 25(OH)D and telomere length (P-interaction = 0.05). Conclusion: Higher plasma 25(OH) D may be associated with longer telomeres, and this association may be modified by calcium intake.

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ONE-CARBON METABOLISM FACTORS AND LEUKOCYTE TELOMERE LENGTH. *Jason Liu, Jennifer Prescott, Edward Giovannucci, Susan Hankinson, Bernard Rosner, Immaculata De Vivo (Department of Epidemiology, Harvard School of Public Health, Boston MA 02115)

Background: Dietary and genetic factors involved in the one-carbon metabolism pathway may affect telomere length through DNA methylation and synthesis, but this has not been comprehensively investigated in epidemiologic studies. We cross-sectionally examine the associations between dietary and genetic factors in the one-carbon metabolism pathway and relative peripheral blood leukocyte telomere length. Methods: 1,715 participants from the Nurses' Health Study (NHS) had measurements of relative telomere length and plasma levels of folate, vitamin B6, vitamin B12, cysteine, and homocysteine. Food frequency questionnaire (FFQ) measurements were also used for assessing folate, choline, methionine, vitamin B2, vitamin B6, vitamin B12, and alcohol intake. Genotyping was performed on 475 participants with a telomere measurement on 29 mostly non-synonymous single nucleotide polymorphisms (SNPs) involved in one-carbon metabolism. The unconditional logistic and linear regression models were used. Results: There were no significant dose-response relationships between any of the plasma or FFQ measured dietary factors and relative telomere length in the multivariate analyses. For folate, vitamin B6, and vitamin B12, the results from using the FFQ data were consistent with the plasma biomarker findings. We found no significant associations involving the SNPs and relative telomere length after accounting for the false discovery rate. Conclusion: Our analyses involving plasma and questionnaire measurements of one-carbon metabolism factors show that some of the key dietary and genetic factors in this metabolic network are not associated with relative peripheral blood leukocyte telomere length.

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IRON STATUS AMONG PRIMARY SCHOOL CHILDREN IN MOROCCO. *Mohamed EL Hioui, Fatima-Zahra Azzaoui, Ahmed Ahami, Stéphane Rusinek, Youssef Aboussaleh, Ahmed Ahami (Faculty of Science, IBN TOFAIL University, Kenitra, Morocco, Kenitra Morocco)

Aims: The objectives of this study were to determine iron Status and Relations between the hematologic profile in Rural School Children in Kenitra. Methods: 295 pupils aged from 6 to 16 years old composed the study group. Blood samples were collected for measuring haemoglobin (Hb), serum ferritin (SF), serum iron and other haematological indices, and subjects were screened for anaemia and iron deficiency. Results: Iron deficiency was found in 20.4 % of the children and the prevalence of iron deficiency anaemia was 7.7%. The mean ferritin level was 27.26 µg/l ± 16.88 whereas the mean serum iron 2.4 mg/l ± 1.0 and the mean haemoglobin concentration was 12.45 g/dl ± 1.02. Associations between Hb concentration, Iron and SF data were evaluated using regression analysis. There were significant correlations between the levels of Hb and SF, mean corpuscular volume (MCV) and SF were found to be significantly related to Hb by stepwise multiple regression analysis. Serum ferritin (SF), serum iron concentrations and MCV were significantly related to Hb level. The overall F-ratio for all variables was 15.04 (df = 3) and was highly significant (P = 0.000). Conclusion: iron deficiency a common problem in the young children particularly the primary education schoolboys of the households of low income. The results of our study suggest that, anaemia can be explained only by iron deficiency.

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URINE LEVEL OF IODINE AND IODIZED SALT USE AMONG SCHOOL CHILDREN AGED 8 TO 10 YEARS IN EASTERN CHINA. *Meifang Su, Qi Zhao, Songtao Li, Xuhua Ying, Yue Chen, Chaowei Fu, Qingwu Jiang (Yuhuan County Center for Disease Control and Prevention, Yuhuan Zhejiang China)

Objective: Both high and low levels of iodine may impair human health, especially for children. The study was to determine the current iodine status of children and its association with iodized salt consumed. Methods: In 2012 we conducted a cross-sectional study in a primary school of Yuhuan County, Zhejiang Province, and 449 out of 450 eligible subjects 8 to 10 years of age provided samples of morning urine and salt consumed in the household. The levels of urine iodine and iodine in salt were measured. Median and inter-quartile range (IQR) were used to describe the levels of urine and salt iodine. Results: The median level of urine iodine was 114.0 µg/L (IQR: 84.4-162.5 µg/L) (boys: 113.5, IQR: 86.0-161.5 µg/L; girls; 115.0, IQR: 81.0-166.0 µg/L). The proportions of subjects with urine iodine <50, 50-99, 100-99, 200-299 and ≥300 µg/L were 4.4%, 37.9%, 47.0%, 12.5% and 2.7%, respectively. There were 447 salt samples with a median of iodine being 0.0 mg/kg (IQR: 0.0-25.0 mg/kg). Only 27.3% of subjects consumed salt with fortified iodine. Children who consumed iodized salt had a significantly higher level of urine iodine than those who did not consume iodized salt (138 vs. 108 µg/L, Z = 3.47, P = 0.001). The proportions of urine iodine <100 µg/L were 29.5% and 40.6%, respectively (Chi-2 = 4.66, P = 0.031), and the proportions of urine iodine ≥200 µg/L were 21.3% and 12.9% (Chi-2 = 4.84,P = 0.028). Conclusion: Majority of the school children showed an adequate level of iodine. Some individuals had an insufficient iodine intake and should be advised to take iodized salt. Key words Cross-sectional study; Urinary iodine; Iodized salt; School children

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INTAKE OF ANTIOXIDANTS AND SUBSEQUENT DECLINE IN PHYSICAL FUNCTION. *Benedetta Bartali, Teresa Curto, Nancy Maserejian, Carrie Wager, Andre Araujo (New England Research Institutes, Inc., Watertown MA 02472)

Oxidative stress is considered a risk factor for declines in physical function (PF) with aging. The objective of this study was to examine the relation of antioxidant intake to change in self-reported PF over a 5-year period. The Boston Area Community Health (BACH) Survey is a population-based longitudinal study of a racially/ethnically diverse population. Change in PF from baseline (2002-2005) to follow-up (2006-2010) was assessed using the SF-12 questionnaire. Intake of antioxidants (combining dietary and supplemental) was estimated at baseline using the validated Block Food Frequency Questionnaire (FFQ). In total, 2828 persons aged 30-79 years completed the FFQ at baseline and participated in the follow-up study. Generalized linear models were used to examine the association between energy-adjusted quartiles of vitamins E, C and carotenoids and change in PF, after adjustment for potential confounders. A low (first quartile) of vitamin E was associated with a greater decline in PF compared with the highest quartile, with an adjusted mean difference in change in PF of -1.73 (95% Confidence Interval (CI):-3.31,-0.15). Notably, this mean difference was equivalent to the effect estimate we found for participants who were approximately 15 years apart in age in our cohort, as 1 year increase in age was associated with a mean difference in change in PF of -0.11 (95% CI:-0.16;-0.06). The results were not statistically significant for vitamin C (mean difference -1.29, 95% CI:-2.61, 0.03) or carotenoids (mean difference = -0.62, 95% CI:-2.22,0.99). Low vitamin E intake was associated with reduced PF with aging. These results extend previous findings that oxidative stress contributes to PF decline and may inform the development of intervention strategies aimed at reducing this clinical and public health problem.

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RELIABILITY OF MEAT, DAIRY, AND EGG INTAKE OVER A 33 YEAR INTERVAL IN ADVENTIST HEALTH STUDY 2. Michael Batech, Pegah Faed, *Karen Jaceldo-Siegl, Marcia Martins, Gary Fraser, Pramil Singh (Loma Linda University, Loma Linda, CA 92350)

Life course epidemiology findings are beginning to identify the importance of dietary intake throughout adulthood on risk of chronic disease. To test such hypotheses in the Adventist Health Study 2 (AHS-2) cohort, our objective was to validate dietary past recall of red meat, poultry, fish, dairy and egg intake in a sample of 3,504 AHS-2 members by comparing past recall with the report of current diet given 33 years earlier during Adventist Health Study 1 (AHS-1). We compared recall of past diet (any intake, weekly intake) at age 30, 40, 50, and 60 years in AHS-2 with the report of current diet at these same ages given 33 years earlier at these ages in AHS-1. Validation of the recall was by calculation of sensitivity (Sn), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), and Spearman's rank correlation coefficients with exact 95% confidence limits. Major findings are as follows: 1) high correlation between the ordinal-scale measures of frequency of diet intake for red meat (range 0.66-0.74), poultry (range 0.47-0.71) and fish (range 0.29-0.63), with lower correlations for dairy (range 0.05-0.23) and eggs (range 0.23-0.31); 2) good validity of any intake of red meat (Sn: 0.70; Sp: 0.92; PPV: 0.91; NPV: 0.73), poultry (Sn: 0.76; Sp: 0.87; PPV: 0.83; NPV: 0.81), fish (Sn: 0.61; Sp: 0.93; PPV: 0.89; NPV: 0.71), dairy (Sn: 0.95; Sp: 0.57; PPV: 0.99; NPV: 0.14), and eggs (Sn: 0.95; Sp: 0.41; PPV: 0.96; NPV: 0.32); 3) validity for weekly intake was lower for red meat (Sn: 0.53; Sp: 0.91; PPV: 0.66; NPV: 0.86), poultry (Sn: 0.59; Sp: 0.84; PPV: 0.22; NPV: 0.97), fish (Sn: 0.26; Sp: 0.94; PPV: 0.25; NPV: 0.95), dairy (Sn: 0.86; Sp: 0.55; PPV: 0.98; NPV: 0.15), and eggs (Sn: 0.75; Sp: 0.48; PPV: 0.70; NPV: 0.54). Intake of red meat, poultry, and fish, an important factor in faith-based diet recommendations in Adventists, was recalled well across three decades in AHS-2. Reliability of recalled dairy and egg consumption was lower.

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DIFFERENCE BETWEEN 24-HOUR DIET RECALL AND URINE EXCRETION DATA FOR ASSESSING POPULATION SODIUM INTAKE IN ADULTS AGED 18-39 YEARS. *Carla Mercado, Mary Cogswell, Amy Valderrama, Chia-Yih Wang, Catherine Loria, Alanna Moshfegh, Donna Rhodes, Alicia Carriquiry (Centers for Disease Control and Prevention, Atlanta GA 30341)

US sodium intake is currently monitored using 24-hour dietary recalls. To assess differences in dietary and urine data in estimating group sodium intake we used data from 185 men and 221 women aged 18-39 years (~50% African-American) participating in a 2011 study in the DC metropolitan area. Dietary sodium intake was estimated using 24-hour dietary recalls (Automated Multiple-Pass Method) and urine sodium excretion using 24-hour urine collection. Using a second measure collected from 1/3 of the participants 4-11 days later, the population percentiles of usual diet and urine sodium were estimated using Software for Intake Distribution Estimation (PC-SIDE, Iowa State University, Ames, Iowa). Mean usual dietary sodium was greater (4895 mg/d men, 3558 mg/d women) than usual urine sodium (3929 mg/d men, 3435 mg/d women). Mean differences in measures were higher in men (927.5 [95% confidence intervals, 779.3, 1075.8] mg/d) than women (111.0 [14.7, 207.3]). Population percentiles distributions for usual dietary sodium and urine sodium were significantly different for men and not for women. Pearson correlations between diet and urine sodium were 0.13 for men and 0.33 for women. Results did not differ by race or age or when excluding individuals who failed to meet expected creatinine excretion criterion. Low correlation and large differences between measures may be due to a lack of correspondence in the reference periods for the recall and urine collection in addition to measurement error in one or both measures.

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BODY SIZE IN RELATION TO URINARY ESTROGENS AND ESTROGEN METABOLITES (EM) AMONG PREMENOPAUSAL WOMEN DURING THE LUTEAL PHASE. *Jing Xie, A Heather Eliassen, Xia Xu, Charles Matthews, Susan Hankinson, Regina Ziegler, Shelley Tworoger (Harvard School of Public Health, Boston MA 02115)

Estrogen metabolism profiles may play an important role in the relationship between body size and breast carcinogenesis. Previously, we observed inverse associations between current body mass index (BMI) and plasma levels of parent estrogens (estrone and estradiol) among premenopausal women during both follicular and luteal phases. Using data from the Nurses' Health Study II, we assessed whether height, current BMI, and BMI at age 18 were associated with the urinary concentrations of 15 estrogens and estrogen metabolites (jointly referred to as EM) measured during the luteal phase among 603 premenopausal women. We observed inverse associations with total EM for height (P (trend) = 0.01) and current BMI (P (trend) = 0.01), but not BMI at age 18 (P (trend) = 0.26). Six EMs were 18-27% lower in women with a height 68+ versus ≤62 in., primarily in the methylated catechol pathway (P (trend) = 0.04). Eight EMs were 18-50% lower in women with a BMI of 30+ versus <20, primarily in the 2-catechol and methylated catechol pathways (P (trend) < 0.001 for both). Our results suggest that height and current BMI are associated with estrogen metabolism profiles in premenopausal women. Further studies with timed urine and blood collections are required to confirm and extend our findings.

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OBESITY AND ASSOCIATED ADVERSE HEALTH OUTCOMES AMONG US MILITARY MEMBERS. *Toni Rush, Cynthia LeardMann, Nancy Crum-Cianflone (Naval Health Research Center, San Diego CA 92106)

Obesity rates have risen over the past two decades, however little data exist regarding the rates of obesity among US military members utilizing a population-based sample of all service branches and components, and its impact on health and service-related outcomes. This study used data from the Millennium Cohort, the largest population-based military study, to assess the prevalence of obesity and the associations of body mass index (BMI) with various health outcomes. Descriptive statistics were performed, and univariate and multivariable associations analyzed. Of 114,064 current or former service members, 46.6% were overweight and 16.4% were obese in 2007. Among active duty members, 14% were obese and 47% overweight by 2007, whereas among veterans these percentages were 30% and 44%, respectively. Over a 6-year period (2001-2007), individuals demonstrated an increase in obesity from 11% to 23%. Overweight and obese participants were significantly more likely to be older, married, in the Reserve/National Guard, and separated from the service. Hypertension (24.7%), diabetes (4.1%), and sleep apnea (11.9%) were significantly more common among obese individuals compared with under/normal weight participants (4.9%, 0.6%, and 1.8%, respectively, all $p < 0.05$). Obese individuals had significantly higher rates of depression (17.8%) and PTSD (13.6%) than under/normal weight individuals (11.9% and 8.7%, respectively), and had lower mental and physical functional scores (all $p < 0.05$). Previous research from the Cohort have shown significant associations between increased BMI and various medical conditions including coronary heart disease, back pain, plantar fasciitis, and Achilles tendinitis. The high prevalence of obesity and associated adverse health effects indicate an urgent need to enhance strategies to prevent and reduce excess weight gain within the military and veteran populations to ensure a fit military force and promote health after military service.

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USE OF BODY WEIGHTS FROM ELECTRONIC MEDICAL RECORDS: OPPORTUNITIES AND CHALLENGES. *Alyson J Littman, Mary Lou Thompson, Edward J Boyko, David E Arterburn (Veterans Affairs Puget Sound Health Care System, Seattle WA 98101)

Electronic health record (EHR) data provide the opportunity to study body weight changes as predictors and outcomes of disease in large, population-based samples. The aim of this paper is to illustrate challenges and possible solutions of using EHR data on body weights. We conducted a retrospective cohort study in 783 persons with a lower limb amputation (LLA) and a demographically similar sample without an amputation (n = 7781). The primary study aims were to assess variation in 3-year weight trajectories following LLA in Veterans Health Affairs patients, by baseline body mass index (BMI) and amputation level and to compare these trajectories with what they might have been had the amputation not occurred. We encountered the following issues in designing and conducting our study: a) whether to employ a matched or unmatched study design, and if matched, the choice of a non-amputee group comparable to the amputees, b) variability in the frequency of records (e.g., mean/ median number of weight measures were 35/21 and 11/8 in study participants with and without a LLA, respectively, over the 39-month follow-up period), and c) identification of erroneous weight measures. We chose to frequency match non-amputees to the amputees on reference year, age, BMI, and diabetes diagnosis. As some individuals had hundreds of weight measures each year, the sheer volume of the data necessitated that we sample non amputees, and matching was indicated due to concerns about insufficient overlap between the groups in important covariates associated with our outcome. Finally, matching on calendar year provided a starting date for the non-amputees. In addressing b) and c) we exploited the longitudinal nature of the records to determine solutions. Studies such as this are important to shed light on the potential pitfalls of longitudinal studies of weight using EHR data and to open communication channels regarding study design approaches and methods to reduce bias.

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NEIGHBOURHOOD TYPOLOGY BASED ON FEATURES OF THE BUILT ENVIRONMENT AND ASSOCIATIONS WITH ADIPOSITY IN YOUTH. *Tracie Barnett, Yan Kestens, Andraea Van Hulst, Basile Chaix, Melanie Henderson (Concordia University and Centre de Recherche du CHU Sainte-Justine, Montreal QC Canada)

Objective: To identify distinct neighbourhood typologies derived from features of the built environment and examine their association with adiposity among youth aged 8-10 years. Methods: Baseline data from the QUALITY cohort, an ongoing longitudinal study of Quebec youth aged 8-10 years with at least one obese parent were used (n = 512). Built environment features were obtained through systematic observations of neighbourhoods; additional data were derived from a geographic information system (MEGAPHONE). Factors were identified in principal components analysis; cluster analysis was then used to identify distinct neighbourhood typologies. Body mass index (BMI) z-scores were computed based on measured weight and height and using CDC growth curves. Fat mass index (FMI) was computed by dividing total body fat mass (from DEXA) by height in m2. Associations between neighbourhood type and adiposity were examined using multivariate linear regression. Results: Three factors were identified: land use mix/density, busy roads/traffic volume, and pedestrian-friendly support. Five distinct neighbourhood types emerged. Adiposity was highest in the neighbourhood type characterized by low pedestrian support, few traffic calming measures, high traffic volume, and many busy roads (FMI: 1.42 kg/m2 $p < 0.01$; and BMI: 0.43 $p < 0.01$). Other neighbourhood types were not associated with adiposity, after taking parental BMI and neighbourhood socio-economic status into account. Conclusions: Traffic-related features appear to be the dominant characteristic of obesogenic neighbourhoods. Although replication in other contexts and with different populations is warranted, interventions designed to reduce or buffer children's exposure to busy roads and high volumes of traffic may be a promising strategy to reduce obesity.

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LIFE COURSE WEIGHT MEASUREMENTS AND CARDIOVASCULAR BIOMARKERS IN PERSONS AGE 60 AND OLDER: A COMPARISON OF THE UNITED STATES AND COSTA RICA. *David Rehkopf, William Dow, Luis Rosero-Bixby (Stanford University, Stanford, CA 94305)

Despite a tremendous research effort, substantial questions remain about when, where and how obesity matters as a driver of mortality. The majority of studies have been done in developed countries, and have most frequently used only single measurements of obesity (measured as BMI) that are taken in middle to later life. Our current analysis addresses two questions: is current BMI the best predictor of mortality risk, or is weight early in life (at age 25), or maximum lifetime BMI an additional or more important indicator of mortality hazard and, are the associations between these multiple measures of adiposity universal across context as biological risks as theorized currently in the literature, or are they potentially explained by confounding due to social class in developed countries? Data from Costa Rica is from the Costa Rican Study on Longevity and Healthy Aging (CRELES), a longitudinal, nationally representative, probabilistic sample of adults aged 60 and over selected from the 2000 census database (n = 1329 men, n = 1498 women). Data from the United States is from the National Health and Nutrition Examination Survey 1999-2004, restricted to adults aged 60 and over (n = 2411 men, n = 3196 women). As expected, we find strong and statistically significant relationships between HbA1c, HDL cholesterol and Triglycerides with BMI. Despite prior suggestion of important life course impacts on cardiovascular risk markers, we find some support for the impact of early life BMI and maximum lifetime BMI on these risk markers. In both Costa Rica and the United States, in models controlling for attained education, we find that maximum lifetime BMI is most or equally predictive of HbA1c. The population health implications of these findings are that most levels of biomarkers may be reversible with changes in weight later in life, but that for some factors (HbA1c) maximum weight may be more important.

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DISTANCE TO FULL-SERVICE SUPERMARKETS: IS LOCATION OF FOOD DESERT RESIDENTS' SHOPPING ASSOCIATED WITH DIETARY QUALITY? *Tamara Dubowitz, Bonnie Ghosh-Dastidar, Deborah Cohen, Elizabeth Steiner, Robin Beckman, Gerald Hunter, Rebecca Collins (RAND, Pittsburgh PA 15217)

Objective: We examined the associations between healthy food availability, food purchasing and dietary intake of residents of urban food deserts. Methods: The Pittsburgh Hill/Homewood Research on Eating, Shopping and Health (PHRESH) study conducted in-person interviews with a representative sample of households (n = 1372) in two urban neighborhoods without full service supermarkets (FSS). We audited all food venues within the neighborhoods (e.g., mom & pop corner stores, take-out restaurants, gas station convenience stores, discount stores, etc.), as well as audits of the 20 food venues outside both neighborhoods where residents most frequently report shopping. Results: 75% of residents reported doing their major food shopping at a FSS; yet just one in three shopped at the FSS closest to their home. All FSS where residents shopped offered a variety of healthy food options, yet residents had poorer diet quality than the national average. Adjusting for age, gender, household income, educational attainment, marital status, children in the household and frequency of reported shopping, we found that residents who shopped at an FSS for their major food shopping had significant lower dietary quality than those who shopped elsewhere (including Supercenters, Wholesale Clubs, Specialty stores, and Discount stores). Residents who shopped at the nearest FSS had an average HEI about 2 points lower, and residents who shopped at another FSS had an HEI about 1.6 points lower than residents who reported shopping elsewhere. Conclusions: Proximity to a FSS may not increase probability that residents shop there or purchase healthier foods. Initiatives to locate FSS in food deserts may not improve purchase of healthy options and diet. Other measures to enhance food access may warrant attention, including improved availability of competitively priced foods, attention to food store marketing and displays, traffic patterns within neighborhoods, and transportation modes.

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NEIGHBORHOOD BUILT AND SOCIAL ENVIRONMENT CHARACTERISTICS AND FAMILIAL OBESITY. *Andraea Van Hulst, Lise Gauvin, Yan Kestens, Tracie A Barnett (of Social and Preventive Medicine, Université de Montréal, Montreal QC Canada)

We examined associations between characteristics of neighborhood built and social environments and likelihood of obesity among family triads living at the same residential address and explored whether these associations differed between family members. Data were from the baseline wave of QUALITY, an ongoing study on the natural history of obesity in 630 Quebec youth aged 8-10 years with a parental history of obesity. Weight and height were measured in children and both biological parents and body mass index (BMI) was computed. Residential neighbourhood environments were characterised using a Geographic Information System and in-person neighbourhood audits. Principal components analysis was used to identify overarching neighbourhood indicators including poverty, prestige, level of urbanicity, traffic, physical disorder and deterioration, and pedestrian friendliness. Multilevel logistic regressions were used to examine associations between neighbourhood indicators and obesity within family triads while controlling for household-level sociodemographic variables. A total of 417 families were included in the analyses. Families residing in lower and average prestige neighborhoods were more likely to be obese (OR = 1.69, 95% CI: 1.16, 2.44, and OR = 1.52, 95% CI: 1.09, 2.12, respectively) than those residing in higher prestige neighborhoods. Residing in lower traffic neighborhoods was associated with a lower likelihood of obesity (OR = 0.70, 95% CI: 0.50, 0.96). Other indicators such as neighborhood poverty were found to have differential effects within the family. Findings suggest that shared neighborhood exposures including prestige and traffic are associated with greater risk of obesity for entire families whereas other neighborhood exposures may heighten risk of obesity in some but not all family members. The latter may reflect differences in the way in which residential neighborhood environments are exploited by each family member.

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CHILD'S SLEEP PROBLEMS AND RISK OF CHILDHOOD OVERWEIGHT: A LONGITUDINAL STUDY. *Liang Wang, *Arsham Alamian (East Tennessee State University, Johnson City TN 37614)

Several studies have found positive associations between child's sleep problems and risk of childhood overweight, but most conclusions have been based on cross-sectional or one time- point cohort studies. Using the longitudinal data set of National Institute of Child Health and Human Development Study of Early Child Care and Youth Development, this study examined the impact of child's sleep problems at 15 months on the development of childhood overweight from 2 to 15 years of age. Childhood overweight (including obesity)(Body Mass Index ≥ the 85th percentile) was assessed at 24 months, 36 months, 54 months, grades 1, 3, 5-8, and 15 years. In total, 1240 children were included in the final analysis if their weight and height were examined at least once from 2 to 15 years of age. Child's sleep problems were defined according to Zukerman et al. (1987) as, child wakes at least 3 times per night, or the child is awake for at least 1 hour on average per night, or the mother reports "severe" disruption. According to Generalized Estimating Equation (GEE) models, child's sleep problems were found to be associated with a 35% increased risk of childhood overweight from 2 through 15 years of age (odds ratio = 1.35, 95% confidence interval = 1.01-1.82), after adjusting for maternal characteristics (including age at birth, education, poverty level, prenatal smoking status, breastfeeding) and child characteristics (including birth weight and race). This key finding adds to the body of evidence that child's sleep problems may have a long-term impact on the later development of childhood overweight. More longitudinal studies are needed to better understand this relationship and to help develop interventions to prevent the growing obesity epidemic.

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SEASONAL VARIATIONS IN PHYSICAL ACTIVITY AND AOLESCENT WEIGHT CHANGE. *Melanie Kornides, Alison Field (Harvard School of Public Health, Boston MA 37614)

The U.S. Department of Health And Human Services (DHHS) recommends adolescents get 1 hour/day of physical activity. No research has examined the association of seasonal variability in activity and obesity risk. The study objective was to determine how seasonal variability in physical activity is related to adolescent weight and weight change. Self-reported data from 5163 girls and 2964 boys, aged 10 to 17 years, in the Growing Up Today Study were used. Hours per week each season engaged in 17 different types of activity were computed. Activity was examined by individual sports and hours per week of moderate or vigorous activity. The outcome was weight change over a two year period. Differences in percentage of normal versus overweight adolescents meeting DHHS recommendations (>7 hours/week) by season and averaged over the year were assessed. Modified Poisson models were used to evaluate the associations between seasonal physical activity levels and risk for overweight/obesity. Approximately 58% of girls and 70% of boys met DHHS recommendations when activity levels were averaged over the year, but only 31% of girls and 41% of boys met recommendations every season. Fewer overweight youth met the recommendations each season (33% of normal weight vs. 25% of overweight girls, $p < .0001$; 42% of normal weight vs. 36% of overweight boys, $p = .02$). There were not significant differences in the adjusted relative risks (RR) of weight gain among highly versus less active youth averaged over the year or by season. Compared to those who met activity recommendations for 3 or 4 seasons, girls who met recommendations for 1-2 seasons had a 1.27 (95% CI 0.97,1.66) adjusted RR of becoming overweight, and boys had an adjusted RR of 1.02 (95% CI 0.74,1.40). In conclusion, few adolescents are consistently highly active throughout the year. Meeting DHHS activity recommendations may not be sufficient in preventing weight gain in adolescents over a two year period.

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ARE PHYSICAL ACTIVITY OPPORTUNITIES AT SCHOOL ASSOCIATED WITH SELF-REPORTED AND ACCELEROMETRY ESTIMATED PHYSICAL ACTIVITY AMONG ELEMENTARY SCHOOL STUDENTS? *Geetanjali Datta, Daniel Fuller, Andrea Van Hulst, Melanie Henderson, Lise Gauvin, Tracie Barnett (Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Montreal QC Canada)

Background and Aim: Childhood obesity and sedentary lifestyle are increasing public health challenges. School environments provide opportunities for physical activity. We assessed the relationship between school environmental and policy factors with self-reported and accelerometry estimated physical activity (PA) among children aged 8-10 years in Montreal. Methods: We used a subset of baseline data from the QUALITY cohort (N= 372), a study investigating the natural history of obesity among youth with at least 1 obese parent. Cluster analysis was performed on 85 observational ratings of opportunities for PA in 297 schools. Observed features included schoolyard characteristics (4), ground amenities (19), gym floor (7), permanent (6) and non-permanent (16) equipment in the gym, gymnastics equipment (11), circus equipment (10), and principal reported physical education policies (12). A 3 cluster solution was chosen representing low (ref), medium and high school PA opportunities. Body Mass Index percentile (BMI%) was computed based on Center for Disease Control norms and categorized into quintiles. Linear GEE models examined associations between PA opportunities and PA, measured by accelerometer (counts of mod/vig PA/wk) and self-report (min/wk), accounting for clustering of children within schools. Analyses were stratified by sex and BMI% quintiles. Results: No overall associations were observed between school PA opportunities and PA outcomes. In stratified analyses, greater PA opportunities were associated with self-reported PA among girls ($\beta = 18.8$, 95% CI 3.2-34.4) and with self-reported PA among those in the highest BMI quintile ($\beta = 15.3$, 95% CI = 0.5-30.0). Conclusions: Greater school PA opportunities may benefit some subgroups of children who are typically less active. In future studies, the impact of quantity or intensity of opportunity may emerge more broadly by taking quality of installations into account.

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CHILDHOOD OBESITY: INFLUENCE OF PERINATAL DETERMINANTS AND FAMILY SOCIO-ECONOMIC CONTEXT.

*Graça Aparício, Madalena Cunha, João Duarte, Anabela Pereira (Polytechnic Institute of Viseu - Health School (Portugal), Viseu Portugal)

Background: The foundations of a healthy life are structured during prenatal period and gain consistency during the first five years of life, being the child growth and development highly influenced by their familiar context. This study aimed to analyse the influence of obstetric and perinatal determinants and parental socioeconomics context in the children's overweight. Methods: Cross-sectional and observational study comprised of 792 preschool children, average age = 4,39 years old (SD = 0,91) and their parents, living in centre of Portugal. Children's anthropometric evaluation and nutritional classification was based on NCHS reference (CDC 2000), obstetric and perinatal classification on WHO recommendations. Results: Globally 66% were normal weight, 31.3% overweight (12.4% obesity) and 2.7% low-weight, the differences shown to be independent from age and gender of the children. The interplay of obstetric determinants (age, mother's weight at the end of pregnancy, and gestational diabetes), and perinatal (gestational age, birth weight and breastfeeding time) revealed that, only birth weight was significantly correlate with overweight children, namely that 7.4% of overweight children were born large ($\chi^2 = 21.130$, $p = 0.002$), implying that a higher birth weight was associated with increased risk of overweight in childhood with a probability greater than 8 times (OR = 8.486, 95% CI = 2.443 - 29.483) ($\chi^2 = 13.636$, $p = 0.000$). From socio-economic variables (parental age, education and household income), only the mother's age, specifically the youngest, assumes significant effect on children's overweight ($\chi^2 = 8{,}683$; $p = 0{,}034$). Conclusions: Results suggest significant effect of birth weight and mother's age, the youngest ones, on the development of overweight. In periodic health monitoring, become of major importance the valorisation of biologic and familiar's risk factors related to overweight children and to consider intervention programs family-centred.

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PATHWAY ANALYSIS FOR HEALTHY WORKER SURVIVOR BIAS IN A COHORT OF ACTIVELY EMPLOYED ALUMINUM FABRICATION WORKERS.

*Sadie Costello, Daniel M Brown, S Katharine Hammond, Mark R Cullen, Ellen A Eisen (University of California, Berkeley CA 94720)

Healthy worker survivor bias arises when there is a time-varying confounder on the causal pathway. In a cohort of 8290 actively employed aluminum fabrication workers followed from 1998 to 2009, we conducted a pathway analysis for $PM_{2.5}$ exposure and incident ischemic heart disease (IHD) focused on two risk factors potentially on the causal pathway: incident hypertension and diabetes. For bias to occur, the three necessary associations are A) prior exposure and the risk factors, B) the risk factors and subsequent exposure, and C) the risk factors and outcome. There were 449 cases of IHD, 2402 cases of hypertension and 859 cases of diabetes. Modeled as a continuous variable (mg/m^3), prior $PM_{2.5}$ predicted hypertension (adjusted odds ratio (OR): 1.04 (95% confidence Interval (CI): 1.01, 1.06)) but not diabetes. Hypertension diagnosis was associated with a 0.01 mg/m^3 reduction (standard error 0.006) and diabetes diagnosis was associated with a 0.02 mg/m^3 (standard error 0.01) reduction in subsequent $PM_{2.5}$ exposure. Hypertension and diabetes were both strong risk factors for incident IHD: the OR for hypertension was 1.96 (CI: 1.60, 2.40) and for diabetes was 2.60 (CI: 2.02, 3.26). Evidence suggests that hypertension, but not diabetes, may be on the causal pathway between $PM_{2.5}$ exposure and IHD. There is modest evidence that hypertension may also be a confounder, thus g-methods are needed to reduce healthy worker survivor bias. In addition, both risk factors predicted leaving work before the age of 60 (censoring) with an OR of 1.36 (CI: 1.19, 1.94) and 1.30 (CI: 1.07, 1.57), for hypertension and diabetes, respectively. To address this potential selection bias, we will need to incorporate censoring weights in all future analyses of $PM_{2.5}$ exposure and IHD.

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LEFT TRUNCATION BIAS IN A COHORT OF ACTIVELY EMPLOYED ALUMINUM FABRICATION WORKERS.

*Sadie Costello, Daniel M Brown, S Katharine Hammond, Mark R Cullen, Ellen A Eisen (University of California, Berkeley CA 94720)

Left truncation occurs when subjects who otherwise meet entry criteria do not remain observable for a later start of follow-up. In occupational studies, those who left work before the start of follow up may have been more susceptible to the health effects of exposure than those who stayed. Including only those who remained at work until the start of follow up can therefore result in a downward bias. We compared associations between cumulative exposure to $PM_{2.5}$ and incidence of ischemic heart disease (IHD) in the full cohort of male fabrication workers followed from 1996 to 2009 and the subset hired after the start of follow up. There were 387 cases (mean age 54) among the full cohort of 6213 workers employed before or after 1996 and 50 cases (mean age 50) among the 1764 (28%) hired after 1996. There was no association between cumulative $PM_{2.5}$ and IHD in the full cohort; adjusted hazard ratios (HR) ranged from 1.13 in the lowest to 0.96 in the highest exposed quintile with all confidence intervals including the null. By contrast, when we excluded subjects hired before start of follow-up, we observed a monotonic increase in the HR across quartiles of cumulative exposure. Relative to the reference group (<0.70 mg/m^3-years), the HRs were 1.11, 1.24 and 1.78, though all confidence intervals included the null. An increase of one in the natural log of $PM_{2.5}$ was associated with a 17% increase in IHD (95% confidence interval: 0.93, 1.47) among those hired after the start of follow up. Although statistical power was compromised by the smaller sample size, younger age and shorter work tenure, restricting to workers hired after the start of follow up appeared to reduce left truncation bias and suggested an increased risk of IHD with increased cumulative exposure.

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RACIAL DISPARITIES IN SHORT SLEEP DURATION BY OCCUPATION AND INDUSTRY.

*Chandra Jackson, Susan Redline, Ichiro Kawachi, Frank Hu (Harvard School of Public Health, Boston MA 02215)

Background: Short sleep, associated with increased morbidity and mortality, has been shown to vary by industry and occupation among US workers, but few studies have investigated Black-White differences in these relationships. Objective: To examine racial/ethnic differences in short sleep duration by industry of employment, we used data from a nationally representative sample of US adults reporting short sleep (n = 41,088) in the National Health Interview Survey from 2004-2011. Methods: Short sleep duration was self reported and categorized as ≤6 hours of usual sleep in a 24 hour period. We estimated prevalence ratios for short sleep duration in Blacks compared to Whites for each industry using Poisson regression models with robust variance estimators adjusting for age, sex, body mass index, and other covariates. Results: Participants' mean age was 49 years, 49% were women, 16% were black, and 24% (25 for whites; 18 for blacks) had at least a college education. Blacks were more likely to report short sleep duration than whites (37 vs. 28%). Compared to whites, adjusted short sleep duration was significantly more prevalent in blacks employed in the following industries: Finances/Information/Real estate (prevalence ratio (PR) = 1.51 [95% confidence interval (CI): 1.35-1.70]), Professional/Administrative/Management (PR = 1.47 [95% CI: 1.31-1.64]), Education (PR = 1.44 [95% CI: 1.28-1.63]), Public administration/Other services (PR = 1.33 [95% CI: 1.21-1.46]), Health care and social services (PR = 1.22 [95% CI: 1.12-1.34]), and Manufacturing/Construction (PR = 1.15 [95% CI: 1.08-1.23]). Short sleep was not different between Blacks and Whites in Retail (PR = 0.99) and Accommodation and food services (PR = 1.00). Conclusions: Black-White differences in short sleep duration varied by industry of occupation, and these findings suggest the need for further investigation of racial/ethnic differences in the work-sleep relationship.

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RESIDENTIAL AND OCCUPATIONAL EXPOSURE TO WOOD TREATING OPERATIONS AS RISK FACTORS FOR BLADDER CANCER. *Lauren E Johns, Jennifer S Pierce, Anders Abelmann, Brent L Finley (ChemRisk LLC, Chicago IL 60602)

There are hundreds of former and currently active wood treatment facilities in the United States, and over time concerns have been raised regarding the potential chronic health effects associated with wood treating-related exposures. In at least one case it has been suggested that there might be an association between risk of bladder cancer and exposure to chemicals associated with historical wood treating operations (creosote, coal tar, and pentachlorophenol) as well as chemicals that may be present at trace levels in these wood-treating agents (polychlorinated dibenzo-p-dioxin and dibenzofurans, benzene, and polycyclic aromatic hydrocarbons). A literature search was conducted to identify all published and unpublished analyses that assessed risk of bladder cancer in (1) residents of communities surrounding wood treating operations (2) wood treating workers, and (3) non-wood treating workers exposed to chemicals potentially associated with wood treating operations. A total of 9 studies that evaluated residents of communities surrounding wood treatment plants, and 4 studies of wood treating workers were located; none of these investigations reported a statistically significantly increased risk of bladder cancer. Additionally, 63 studies were located that evaluated non-wood treating workers exposed to chemicals potentially associated with wood treating operations, of which 3 reported a statistically significantly increased risk of bladder cancer. However, in one of these studies, the elevated risk was attributed to exposure to aromatic amines, and in the other two studies, there was no attempt to control for smoking in terms of pack-years (smoking is a significant risk factor for bladder cancer). We conclude that the weight of evidence indicates no association between residential or occupational exposure to wood treating operations and risk of bladder cancer.

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COMBAT EXPERIENCES AND MULTIPLE DEPLOYMENTS ARE RISK FACTORS FOR MOTOR VEHICLE CRASHES. *Kelly Woodall, Isabel Jacobson, Nancy Crum-Cianflone (Naval Health Research Center, San Diego CA 92106)

Although rates of motor vehicle fatalities have fallen among both military personnel and civilians over the last several decades, motor vehicle crashes (MVCs) continue to account for a third of US military fatalities each year. Sociodemographic factors associated with MVCs among service members have been evaluated, but whether specific war-time experiences of the current operations are associated with a higher risk of MVCs is unclear. Data from the Millennium Cohort Study and the Medical Data Repository were utilized to investigate MVCs occurring six months post-deployment in relation to service-related factors while adjusting for behavioral and physical health, and demographic characteristics. Active-duty participants who enrolled in the Cohort during 2001-2006 and had not separated from the military prior to their baseline survey were included in this study. Cox proportional hazards modeling was used for analysis. After exclusions, 13,620 deployed personnel were included, with 0.8% having a MVC within six months post-deployment. After adjusting for covariates, those with combat experiences (hazard ratio (HR) = 1.86, 95% confidence interval (CI): 1.33-2.62) and those with more than 1 deployment (2 deployments HR = 1.93, 95% CI: 1.32-2.83; 3 or more deployments HR = 2.83, 95% CI: 1.71-4.67) were significantly more likely to have a MVC within six months post-deployment. In addition, enlisted vs. officers had a higher risk for a MVC. Experiencing combat during deployment is a strong predictor for MVCs within six months of returning home among US military members. Stressful events during deployment may enhance post-deployment risk-taking behaviors or may be associated with recurrent emotional thoughts that impair driving. Also, this study demonstrates that multiple deployments are associated with increased risk for MVCs. These data provide critical information for targeting prevention strategies to decrease MVCs among service members returning from deployment.

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A SYSTEMATIC REVIEW AND META-ANALYSIS OF REFINERY WORKERS AND RISK OF MESOTHELIOMA. *Meg McKinley, Lauren Roberts, Rebecca Ward, Sara Gale, Zachary Capshaw, Grace Anderson, Connie Chen, Christy Barlow (Cardno-Chemrisk, San Francisco CA 94105)

Mesothelioma has traditionally been associated with occupational asbestos exposures in the insulating, shipbuilding, welding, sheet metal, and pipefitting industries. Petroleum refineries employ a variety of workers who experience different potentials for asbestos exposure depending on job tasks. To date, a systematic review and meta-analysis of the mesothelioma risk for petrochemical/refinery workers has not yet been conducted. We reviewed over one hundred studies of mesothelioma mortality patterns published in the peer-reviewed literature and identified 16 cohort studies that presented mesothelioma relative risk (RR) estimates for refinery workers in the United States, Italy, Canada, and Australia. Follow-up times spanned from 1914 to 2003, but a majority of the study population was employed between 1945 and 1990. Overall, effect measures ranged 0.32 to 16.63, and 9 of the RR estimates were statistically significant for a positive association between the general category of refinery workers and mesothelioma. There were 7 studies that presented a RR estimate specific to sub-populations of refinery workers including maintenance, trades, or hourly workers; these effect measures ranged from 2.0 to 16.63. All but one of these was statistically significant for a positive association. A meta-RR estimate for the general category of refinery workers was 3.32 (95% CI: 2.88-3.84). A meta-RR estimate for the aforementioned sub-population of refinery workers was higher (5.11; 95% CI: 4.17-6.28). Although there is variability of work-related exposures that might occur among workers that are broadly defined as refinery employees, workers in the trades and general maintenance workers likely experience the most substantial opportunities for asbestos exposure due to work with or near insulation; these sub-populations also experience increased mortality due to mesothelioma.

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SELF-REPORTED HEARING LOSS IN THE MILLENNIUM COHORT. Timothy Wells, *Amber Seelig, Margaret Ryan, Jason Jones, Tomoko Hooper, Edward Boyko (Naval Health Research Center, San Diego CA 92106)

The purpose of this research was to characterize new-onset hearing loss in a large military cohort and to determine whether combat deployment is associated with hearing loss. Data were from the Millennium Cohort Study, a military cohort, collected from 2001-2008 (n = 57,533). Using multivariable logistic regression models, new-onset, self-reported hearing loss was assessed in relation to combat experiences, while adjusting for relevant demographic, military, and behavioral covariates. A total of 3,899 (6.8%) participants self-reported new-onset hearing loss during follow-up. Combat deployers had increased odds [Adjusted Odds Ratio (AOR): 1.73, 95% Confidence Interval (CI) 1.60, 1.88] of reporting hearing loss compared with nondeployers, while non-combat deployers did not have a higher odds (AOR 0.98, 95% CI 0.88, 1.08). Subanalyses among deployers showed that those reporting combat-related head trauma had a 6-fold odds (AOR 6.89, 95% CI: 4.07, 11.60) of reporting hearing loss compared to deployers without a head trauma. Additionally, reporting exposure to an IED blast was associated with 2.12 (95% CI: 1.66, 2.71) greater odds of reporting new-onset hearing loss compared to deployers who did not report an IED blast. Although we were not able to measure other specific exposures like impulse noises from firing weapons or the detonation of explosive devises, future studies should further examine the pathophysiology of combat-related hearing loss and prevention strategies.

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QUANTIFYING THE POTENTIAL IMPACT OF MEASUREMENT ERROR IN THE EARLY AUTISM RISK LONGITUDINAL INVESTIGATION (EARLI). *Karyn Heavner, Craig Newschaffer, Irva Hertz-Picciotto, Deborah Bennett, Igor Burstyn (Drexel University, Philadelphia PA 19102)

EARLI, an ongoing study of a risk-enriched pregnancy cohort, examines genetic and environmental risk factors for autism spectrum disorders (ASD). We simulated the potential effects of measurement error (ME) and misclassification of exposures and autism endophenotype (Autism Observation Scale in Infants (AOSI) scores) on measures of association generated under this study design. We investigated the impact on the power to detect true associations with exposure and the false positive rate (FPR) for a non-causal correlate of exposure (×2, r = 0.7) for continuous AOSI score (linear model) versus dichotomized AOSI (logistic regression) when the sample size (n), degree of ME in exposure, and strength of the true association (target odds ratio (tOR)) between exposure and AOSI varied. Exposure was a continuous variable in all linear models and dichotomized at 1 standard deviation above the log-mean in logistic models. Simulations reveal complex patterns and suggest that: 1) There was attenuation of associations when the tOR increased from 1.5 to 4, even though the ME is differential due to dichotomization of miss-measured variables; 2) Logistic regression had much lower power than the linear models (e.g. for n = 400 and tOR = 2, when ME is half of the true exposure variance, power is 85% and 39% in linear and logistic models, respectively); 3) The proportion of samples in which ×2 was associated with AOSI score was considerable under most scenarios (e.g. for n = 400 and tOR = 2 in linear models, it increased from 6 to 31% as ME increased); and 4) The FPR has a complex dependence on the tOR, ME and model choice, but was greater for logistic models. The findings will stimulate work examining cost-effective strategies to reduce the impact of ME in realistic sample sizes (e.g. when individual samples are pooled for exposure quantification) and affirm the importance of investment in biological samples that help precisely quantify a wide range of environmental exposures.

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LOW BIRTH WEIGHT BABIES ARE MORE OFTEN SMOKERS AS ADULTS. *Liv Grimstvedt Kvalvik, Rolv Skjærven, Kari Klungsøyr, Stein Emil Vollset, Kjell Haug (University of Bergen, Bergen Norway)

Background: Low birth weight has been postulated to be a cause of, through early programming, cardiovascular disease in adult life. We suggest that low birth weight also is a marker for maternal smoking during pregnancy, and that these smoking habits will be passed on to next generation. Objective: The aim was to study whether there is a higher prevalence of adult daily smoking among men and women born with low rather than normal birth weight. Material and Methods: We used data from the Medical Birth Registry of Norway (MBRN), which has national coverage of all births since 1967. We studied birth weight of term, singleton women (n = 172 509) and men (n = 130 927) in 1967-1995, and linked these to their own infants delivered in 1999-2010, where maternal smoking habits during pregnancy were registered. Z-score of birth weight by gestational age in the first generation was exposure and maternal smoking habits of the adult women or the partners of the adult men were outcomes. Results: 20 % of mothers with Z-score -3.5 were daily smokers, compared to 8 % of women with Z-score 1.5 (RR 2.45 (95 % C.I. 1.73 – 3.47)). 15 % of fathers with Z-score -3.5 had a daily smoking partner, compared to 9 % of fathers with a 1.5 Z-score (RR 1.72 (95 % C.I. 1.02 – 2.92)). The relation persisted when stratifying by grandmothers' education (mothers of the first generation infants). Conclusion: Our findings indicate that being born low birth weight is associated with smoking in adulthood.

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IMPACT OF UNDER-ASCERTAINING COMORBID CONDITIONS AT DELIVERY ON ESTIMATED DISEASE PREVALENCE IN A PREGNANT POPULATION. *Amy Metcalfe, Lisa Lix, Francois Bernier, Gillian Currie, Andrew Lyon, Jo-Ann Johnson, Suzanne Tough (University of British Columbia, Vancouver BC Canada)

Background: Hospital billing data for delivery is frequently used to assess maternal comorbidity status. Increasing the length of the observation period for identifying comorbidities in hospital billing data can increase ascertainment; however, as many women of childbearing age will not be hospitalized except for delivery this may still under-ascertain the prevalence of comorbid conditions. Methods: Clinical and administrative databases from Alberta Canada were linked to create a population-based cohort of pregnant women who delivered a live or stillborn infant in hospital (n = 6026). Comorbidities were identified in administrative data for the delivery hospitalization and for all health care contacts (hospitalizations, emergency room visits and physician visits) that occurred during pregnancy and three months prior to conception. Results: More than one third (36.7%) of women had at least one health care contact during pregnancy or just prior to conception that indicated the presence of a comorbid condition; approximately one-third of these were not documented the birth hospitalization record. Prevalence estimates increased for all comorbidities when the ascertainment period and number of ascertainment sources increased (i.e. prevalence of asthma increased from 0.2% to 3.1%, prevalence of type 1 or 2 diabetes increased from 0.8% to 5.8%, and prevalence of pre-eclampsia increased from 1.5% to 5.0%). Conclusions: A substantial proportion of comorbidities are not documented during the delivery hospitalization. Prevalence estimates based exclusively on the delivery record systematically under-estimate the frequency of comorbid disease in a pregnant population.

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DISCONTINUATION OF HORMONAL CONTRACEPTION AMONG BLACK FEMALE TEENS ATTENDING AN URBAN FAMILY PLANNING CLINIC. *Michael Lowe, Maura Whiteman, Polly Marchbanks, Melissa Kottke, Peggy Goedken (Centers for Disease Control and Prevention, Atlanta GA 30341)

Over 300,000 infants are born to U.S. teens annually and racial/ethnic disparities persist. Over half of sexually-active teens have used hormonal contraceptives, but little is known about factors associated with discontinuation of these methods. We recruited sexually-active black females ages 14-19 (n = 350) in a publically-funded family planning clinic who responded to an audio computer-assisted self-interview questionnaire collecting information about contraceptive history and sexual behavior. We used multivariable logistic regression to examine factors associated with discontinuing hormonal contraceptive methods. Two thirds of participants (n = 232, 66%) ever used hormonal contraception, most commonly injectable contraception (DMPA) (47%). Half of those who used any hormonal method were no longer using one (n = 119, 51%). Of those who discontinued hormonal methods, 40% used no contraceptive method at last sex. Among participants discontinuing DMPA and oral contraceptives (OCs), perceived body or menstrual cycle changes was a common reason for discontinuation (55% for DMPA, 33% for OCs), while over one-third of those discontinuing OCs cited trouble using them. Characteristics independently associated with discontinuing hormonal methods included having >4 lifetime sexual partners (adjusted odds ratio (aOR): 1.7; 95% confidence interval (CI): 1.0-3.0) and mother's education of less than high school (aOR: 2.6; 95% CI: 1.5-4.9). A broader understanding of hormonal contraception discontinuation among teens will help develop strategies to improve continuation or encourage selection of highly effective user-independent methods, such as intrauterine devices or implants.

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METHODOLOGICAL CHALLENGES OF STUDYING INDUCTION OF LABOR: TIME-DEPENDENT CONFOUNDING BY BIRTHWEIGHT. *Jonathan M Snowden, Michelle C Odden, Yvonne W Cheng, Aaron B Caughey (Oregon Health and Science University, Portland OR 97239)

The evidence regarding the benefit or harm of induction of labor (IOL) is conflicting, and is complicated by the role of birthweight (BW). Recent methodological work has demonstrated the potential bias that controlling for BW may introduce into associations between baseline/antepartum maternal risk factors and neonatal outcomes, due to conditioning on a causal intermediate. However, less attention has been paid to the role of birthweight in studies of intrapartum exposures such as induction of IOL. Intrauterine growth is a strong predictor of the clinical and patient decision to induce labor, and also affects neonatal outcomes, making it a confounder of labor induction's health effects. However, the decision to not induce labor (i.e., expectant management of pregnancy) results in a longer gestation with additional fetal growth and delivery at a later date. This causal structure places BW on the causal pathway between the initial exposure (IOL or expectant management) and neonatal outcomes in the comparison group. We employ Directed Acyclic Graphs (DAGs) to visually depict this time-dependent confounding, representing causal pathways for the exposed group (i.e., IOL) and the unexposed group (expectantly managed pregnancies). Based on the DAGs and the subject matter they encode, we discuss the biases introduced into IOL effect estimates due to the decision to control for BW or not control for BW. The former results in uncontrolled confounding bias, and the latter controls for a causal intermediate. Controlling for estimated fetal weight at index gestational age (i.e., the gestational age of labor induction) would be an appropriate methodological approach, but such data are rarely available in practice. Back-calculating estimated fetal weight at index gestational age assuming constant fetal growth at term is one analytical option. We also discuss the potential application of inverse probability weighting to address this confounding.

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HIGHER IRON INTAKE IN RELATION TO AN INCREASED RISK OF PROGRESSION FROM GESTATIONAL DIABETES TO TYPE 2 DIABETES AFTER THE INDEX PREGNANCY: FINDINGS FROM THE DIABETES & WOMEN'S HEALTH STUDY. *Wei Bao, Katherine Bowers, Deirdre K Tobias, Frank B Hu, Cuilin Zhang (Epidemiology Branch, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Rockville MD 20852)

Women with a history of gestational diabetes mellitus (GDM) are at exceptionally high risk to develop type 2 diabetes mellitus (T2DM) later in life. However, modifiable lifestyle factors that determine T2DM risk among this high risk population are largely unknown. The use of iron supplements in U.S. women has been steadily increased. This study was to examine the associations of dietary and supplemental iron intakes with T2DM risk. As part of the Diabetes & Women's Health Study participants, 4,031 women in the Nurses' Health Study II who had a history of GDM were followed up from 1991 to 2007. Among them, 582 women developed incident T2DM during the 60,200.6 person-years of observation. Multivariable Cox proportional hazards models were used to estimate the relative risks (RRs) and 95% confidence intervals (CIs). After adjusting for age, parity, BMI, other non-dietary and dietary factors, the multivariate RRs for T2DM across increasing quintiles of total iron intake were 1.00, 1.13, 1.17, 1.14, and 1.51 (P for trend = 0.02), and the multivariate RRs across increasing tertiles of supplemental iron intake were 1.00, 1.30, and 1.53 (P for trend = 0.001). Such an association persisted regardless whether supplemental iron was from multivitamins or iron supplement. Dietary iron intake (i.e. heme and non-heme iron) was not significantly associated with T2DM risk. In summary, higher iron intake, particularly supplemental iron intake, is significantly associated with a greater risk of progression from GDM to T2DM.

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PREPREGNANCY LOW-CARBOHYDRATE DIET SCORES AND THE RISK OF GESTATIONAL DIABETES MELLITUS: A PROSPECTIVE COHORT STUDY. *Wei Bao, Katherine Bowers, Deirdre K Tobias, Frank B Hu, Sjurdur Olsen, Jorge Chavarro, Allan Vaag, Cuilin Zhang (Epidemiology Branch, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Rockville MD 20852)

Low-carbohydrate diets (LCDs) have been vastly popularized, despite concerns of their long-term efficacy and safety. Previous studies have examined the individual association of carbohydrate, protein and fat intake with the risk of gestational diabetes mellitus (GDM). However, their combined effect as measured by LCD score on GDM risk remains unknown. Our study included 21,457 singleton pregnancies without chronic diseases before pregnancy or previous GDM in the Nurses' Health Study II between 1991 and 2001. Overall, animal and vegetable LCD scores were calculated from food-frequency questionnaires, with a higher score reflecting a higher intake of protein and fat and a lower intake of carbohydrate. Generalized estimating equations with log-binomial models were used to estimate the relative risks (RRs) and 95% confidence intervals (CIs). We documented 870 incident GDM pregnancies during the 10 years of follow-up. After adjustment for age, parity, non-dietary and dietary factors, and body mass index, prepregnancy overall and animal LCD scores were significantly and positively associated with GDM risk while vegetable LCD score was not significantly associated with the risk. The RRs (95% CIs) comparing the highest with lowest quintiles were 1.59 (1.29-1.96) for overall LCD score, 1.41 (1.15-1.72) for animal LCD score, and 0.82 (0.66-1.02) for vegetable LCD score. These associations were not significantly modified by age, parity, family history of diabetes, or physical activity. In conclusion, a prepregnancy diet with lower carbohydrate and higher protein and fat, in particular protein and fat from animal food sources, is significantly and positively associated with GDM risk.

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WITHDRAWN

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ACETAMINOPHEN USE DURING PREGNANCY AND THE RISK OF BEHAVIORAL PROBLEMS AND HYPERKINETIC DISORDERS IN DANISH CHILDREN. *Zeyan Liew, Beate Ritz, Cristina Rebordosa, Pei-Chen Lee, Jørn Olsen (Department of Epidemiology, Fielding School of Public Health, University of California at Los Angeles, Los Angeles CA 90095)

Background: Acetaminophen is one of the most common pain and fever medications used by pregnant women. In animal studies, acetaminophen has been shown to be acting as a strong hormonal disruptor, and some human evidence indicate that hormone levels during pregnancy may influence behavioral dysfunction in early childhood. We investigate for the first time whether the use of acetaminophen during pregnancy increases the risk of behavioral problem or Hyperkinetic Disorders (HKD) in children. Method: We studied 64,322 liveborn singleton children and mothers first enrolled in the Danish National Birth Cohort (DNBC) during 1997–2002. Use of acetaminophen during pregnancy was assessed in 3 computer-assisted telephone interviews at baseline between 6-12 weeks of pregnancy and 6 months of age of the child. Three different data sources were used to ascertain the outcome. First, we assessed behavioral problems of children at 7 years of age as reported by parents in the Strength and Difficulties Questionnaire (SDQ). Second, prior to end of follow-up in 2011, 834 children received a HKD diagnosis as reported in the Danish National Hospital Registry and the Danish Psychiatric Central Registry. Third, we used information about HKD prescriptions for the children in the DNBC recorded in the national prescription database. Results: Children born to mothers who used acetaminophen during pregnancy were at 10-40% higher risks of receiving a hospital diagnosis of HKD, receiving HKD medications, or having behavioral problems at 7 years of age. Stronger effects for acetaminophen were estimated when mothers used acetaminophen in more than one pregnancy trimesters, and a clear dose response was detected with increasing frequency of acetaminophen use during gestation and HKD diagnosis or medication (p-trend < 0.0001). Conclusion: Maternal intake of acetaminophen during pregnancy may increase the risk of Hyperkinetic Disorders and behavioral problems in children by age seven.

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MATERNAL PSYCHOSOCIAL STRESS AND RISK OF ADVERSE BIRTH OUTCOMES IN A HISPANIC POPULATION OF PREDOMINANTLY PUERTO RICAN WOMEN. *Kathleen Szegda, Elizabeth Bertone-Johnson, Penelope Pekow, Sally Powers, Glenn Markenson, Nancy Dole, Lisa Chasan-Taber (University of Massachusetts, Amherst MA 01003)

Studies of maternal psychosocial stress and preterm birth (PTB), low birth weight (LBW) and small-for-gestational age (SGA) have been inconsistent, with few conducted among Puerto Rican women, a Hispanic subgroup with high rates of these adverse birth outcomes and subsequent infant mortality. We examined these associations among 1,262 Hispanic pregnant women of Puerto Rican or Dominican descent participating in Proyecto Buena Salud (2006-2011), a prospective cohort study conducted in Western Massachusetts. Perceived stress was assessed at prenatal care visits in early (<19 weeks gestation), mid (19-26 weeks gestation), and late (>26 weeks gestation) pregnancy using Cohen's Perceived Stress Scale (PSS-14). PTB (<37weeks gestation), LBW (<2500 grams birth weight), and SGA (<10th percentile birth weight for gestational age) birth status was determined through medical record abstraction; 9.3% of births were PTB, 7.8% were LBW, and 12.4% were SGA. After adjusting for sociodemographic, medical and other psychological factors using multivariable regression analysis, perceived stress in mid-pregnancy was positively associated with PTB (p- trend = 0.004) and LBW (p-trend = 0.007). Compared to women in the lowest quartile, women in the highest quartile of perceived stress in mid-pregnancy had over 3 times the risk of PTB (Odds Ratio [OR] = 3.4, 95% Confidence Interval [CI] = 1.3, 9.0) and LBW (OR = 3.5, 95% CI = 1.3, 9.7). Elevated levels of perceived stress were not associated with SGA, and there was no association between early or late pregnancy perceived stress and PTB or LBW. Cumulative duration of exposure to perceived stress and pattern of exposure over the course of pregnancy were not associated with increased risk for PTB, LBW, or SGA. In this predominantly Puerto Rican population of Hispanic women, exposure to elevated levels of perceived stress in mid-pregnancy increased risk for PTB and LBW.

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FAMILIAL CLUSTERING OF POSTPARTUM HEMORRHAGE IN THE SWEDISH POPULATION. Anna Sara Oberg, Thomas Frisell, Sonia Hernandez-Diaz, Catarina Almqvist, *Brian T Bateman (Department of Epidemiology, Harvard School of Public Health, Boston MA 02115)

Introduction: Postpartum hemorrhage (PPH) is the leading cause of maternal mortality worldwide. A potential inherited predisposition to PPH has not, to our knowledge, been previously described. Making use of national registers of birth and family relations, we therefore explored familial clustering of PPH in the Swedish population. Methods: We considered the deliveries of all full and half-siblings born in Sweden between 1997 and 2009. Alternating logistic regression was applied to model the familial clustering with pairwise odds ratios, and covariates were included to evaluate whether familial clustering could be explained by exposure to shared risk factors. Results: In the eligible N = 466 580 deliveries, overall risk of PPH was 4.4%. Odds of PPH were increased in women with a previous PPH, both with the same partner (Odds ratio (OR) = 4.0, 95% confidence interval (CI): 3.7, 4.3) and after partner change (OR = 3.4, 95% CI: 2.8, 4.2). An affected sibling conferred higher odds of PPH in sisters (OR = 1.5 95% CI: 1.3, 1.8) as well as (partners of) brothers (OR = 1.2 95% CI: 1.1, 1.5). Potential sharing of risk factors for PPH, including maternal age, parity, pre-pregnancy BMI, induction of labor, c-section, postterm birth, and fetal size, had little influence on the estimates. Conclusion: The findings demonstrate a strong maternal influence on the liability of PPH, illustrated by clustering in women irrespective of partner, as well as in sisters. The lower OR in women who change partners compared to those who don't, and clustering in brothers also indicates some paternal influence. Practitioners should assess family history when determining a woman's risk for PPH. Future research is needed to understand the genetic and environmental contributions to the observed tendency to repeat PPH in families.

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SLEEP DISORDERS AND RACE/ETHNICITY IN PREGNANT AND NON-PREGNANT WOMEN OF CHILDBEARING AGE. *Melissa Amyx, Xu Xiong, Pierre Buekens (Tulane University School of Public Health and Tropical Medicine, New Orleans LA 70112)

The authors sought to examine the association between sleep disorders and race/ethnicity in both pregnant and non-pregnant women of child-bearing age. Self-reported health and sleep characterestics collected by the National Health and Nutrition Examination Survey (NHANES) from 2005 to 2010 were used to conduct this secondary analysis. The present study sample included 3,875 non-pregnant and 507 pregnant women from 15 to 44 years of age. The association between sleep disorders and race/ethnicity was examined using both univariate and multivariate logistic regression, adjusting for age, body mass index, marital status, education, and other confounding variables. In non-pregnant women, the prevalence of trouble sleeping was 22.30% among Mexican-American women, 22.31% among non-Hispanic white women, and 23.05% among non-Hispanic black women; in pregnant women, the prevalences were 17.43%, 29.41%, and 14.55%, respectively. After adjustment for confounders, the significantly decreased risk of trouble sleeping in pregnant Mexican-American and non-Hispanic black women when compared to pregnant non-Hispanic white women persisted, with adjusted odds ratios (aOR) of 0.415 (95% confidence interval 0.173, 0.993) and 0.204 (0.064, 0.647), respectively. Among non-pregnant women, risk did not differ by race/ethinicity (aORs 1.014 [0.758, 1.357] and 1.006 [0.757, 1.337], respectively). We conclude that trouble sleeping is associated with race/ethnicity among pregnant women, but not non-pregnant women, of childbearing age.

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INTERACTION BETWEEN MATERNAL PASSIVE SMOKING DURING PREGNANCY AND CYP1A1 AND GSTT1 POLYMORPHISMS ON FULL TERM LOW BIRTH WEIGHT. *Wei-Qing Chen, Peng Ding, Xiaozhong Wen, Cai-xia Zhang, Yi-juan Luo, Shi-Xin Yuan, Xiao-Ling Guo (Department of Medical Statistics and Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou Guangdong China)

Objectives: To examine interactions between maternal passive smoking during pregnancy and CYP1A1 and GSTT1 polymorphisms on risk of full term low birth weight (LBW). Methods: We conducted a case-control study among 233 Chinese women with the full term LBW and 677 with normal births in Guangdong, Southern China. Maternal self-report and serum cotinine concentration (3 ng/ml) were combined to define maternal passive smoking during pregnancy. The single nucleotide polymorphisms of CYP1A1 M1 (TT, TC, CC), CYP1A1 M2 (AA, AG, GG), and GSTT1 (null vs. present) were tested by PCR-RFLP sequencing approaches. Logistic regression model was used to test gene-environmental interactions, adjusting for maternal age, occupation, education, pre-pregnancy body weight, and family income. Results: Passive smoking during pregnancy was associated with higher risk of full term LBW (adjusted odds ratio, 2.27 [1.68-3.09]). We found two-way interactions between passive smoking and CYP1A1 M1 CC (5.83 [1.79-19.00]; vs. CYP1A1 M1 TT) or GSTT1 null (5.24 [2.72-10.09]; vs. GSTT1 present), on risk of full term LBW. There were also two-way interactions between CYP1A1 M1 TC or CC and GSTT1 null. We also found three-way interactions among passive smoking, CYP1A1 M1 TC (5.83 [1.79-19.00]), and GSTT1 null (6.00 [1.52-23.61]; vs. CYP1A1 M1 TT). Similar, there were three-way interaction among passive smoking, CYP1A1 M2 AG (9.54 [2.32-39.28]; vs. CYP1A1 M2 AA) or CYP1A1 M2 GG (114.73 [4.45-2414.29]; vs. CYP1A1 M2 AA), and GSTT1 null. Conclusion: In our sample, maternal passive smoking during pregnancy interacted with maternal CYP1A1 and GSTT1 genotypes on risk of full term LBW.

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PERTURBATIONS IN TESTOSTERONE ARE ASSOCIATED WITH SPORADIC ANOVULATION IN NORMALLY MENSTRUATING WOMEN. *Lindsey Sjaarda, Sunni Mumford, S Katherine Laughon, Kerri Kissell, Jean Wactawski-Wende, Enrique Schisterman (Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda MD 20892)

Hyperandrogenism is a hallmark of polycystic ovary syndrome (PCOS) in women with irregular menses, yet its relationship to ovarian function and ovulation remains poorly understood. This study evaluated whether elevated testosterone, and other related endocrine perturbations usually associated with PCOS, were evident in the anovulatory (n = 42) versus ovulatory (n = 467) cycles of normally menstruating, premenopausal women without a self-reported history of PCOS (n = 259, ages 18-44). Blood samples were collected ≤ 8 times per cycle for ≤ 2 cycles per woman with visit timing assisted by fertility monitors. Repeated measures analysis of variance was conducted on log-transformed data with adjustment for age. Total testosterone varied over the cycle ($P < 0.001$), with the highest concentration (mean ± SE: 36.0 ± 0.9 ng/dL) near ovulation. Testosterone increased from menses to ovulation/mid-cycle by 81.1 ± 2.8% in ovulatory compared to 69.4 ± 12.0% in anovulatory cycles ($P = 0.3$). The subsequent decline in total testosterone from ovulation to the late luteal phase was greater in ovulatory (39.3 ± 0.6%) than anovulatory (21.5 ± 2.9%, $P < 0.001$) cycles. Compared to ovulatory cycles, anovulatory cycles exhibited greater testosterone (33.6 ± 0.6 vs. 29.7 ± 0.2 ng/dL, $P < 0.001$) and lower sex hormone binding globulin (SHBG; 43.7 ± 1.3 vs. 48.7 ± 0.4 nmol/L, $P < 0.001$), in addition to greater luteinizing hormone (LH): follicle-stimulating hormone (FSH) ratio around menses (1.0 ± 0.2 vs. 0.7 ± 0.1, $P < 0.001$) and lower LH:FSH ratio prior to ovulation (1.5 ± 0.2 vs. 3.2 ± 0.1, $P < 0.001$). In conclusion, anovulation in normally menstruating women is associated with altered testosterone, SHBG and LH:FSH ratio, lending evidence that ovulatory impairment may exist along a continuum of androgen excess.

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VISION IMPAIRMENT, HEARING LOSS AND CO-OCCURRING AUTISM SPECTRUM DISORDERS IN CHILDREN. *Vijaya Kancherla, Kim Van Naarden Braun, Marshalyn Yeargin-Allsopp (Centers for Disease Control and Prevention, Atlanta GA 30333)

Limited population-based data on prevalence and determinants of childhood vision impairment (VI) and hearing loss (HL), and their co-occurrence with autism spectrum disorders (ASD) exist. The objectives of our study were to 1) estimate population-based prevalence of VI, HL and co-occurrence with ASD among 8-year-olds living in metropolitan Atlanta during 2000-2008; and 2) examine birth and parental characteristics, and the presence and severity of other developmental disabilities among children with VI and HL, by co-occurring ASD. We used data from the Metropolitan Atlanta Developmental Disabilities Surveillance Program, a population-based multiple-source surveillance system for developmental disabilities among 8-year-olds. Both VI and HL prevalence was 1.2 per 1000 8-year-olds. Prevalence was higher among boys and Hispanic children for VI and HL. Approximately 6-7% of children with VI or HL had co-occurring ASD. Children with VI or HL with co-occurring ASD differed from those without co-occurring ASD by select birth characteristics and the presence of other developmental disabilities, such as intellectual disability or cerebral palsy. The median age of earliest known ASD diagnosis by a community provider was significantly greater in children with VI and co-occurring ASD compared to children with ASD but without VI (77 months vs. 56 months, $p = 0.02$). While the median age of earliest known ASD diagnosis did not differ for children with HL and ASD compared to those with ASD without HL, unlike VI, the age at which children with HL and ASD were first evaluated by a community provider was significantly earlier than those with ASD without HL (39.5 months vs. 50 months, $p = 0.01$). The significant delay in ASD diagnosis in children with VI compared to those without VI highlight the importance of developing appropriate screening tools for early identification of ASD among children with VI. ASD diagnosis may be made earlier among children with HL and ASD.

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CHALLENGES TO CREATING A NATIONWIDE SURVEILLANCE SYSTEM FOR CHRONIC KIDNEY DISEASE. *Laura Plantinga, Charles McCulloch, Rajiv Saran, Elizabeth Hedgeman, Sharon Saydah, Meda Pavkov, Neil Powe, for the CDC CKD Surveillance Team (Emory University, Atlanta GA 30322)

Chronic kidney disease (CKD) affects at least 1 in 10 U.S. adults and increases the risk for mortality, cardiovascular events, and costly end-stage renal disease (ESRD). In October 2006, the Centers for Disease Control and Prevention (CDC) charged our team with the creation of a nationwide surveillance system that could provide comprehensive epidemiologic pre-ESRD CKD data. Over the next 6 years, in conjunction with an expert Advisory Group, we created a publicly available, web-based surveillance system (www.cdc.gov/ckd/surveillance). In addition to addressing the key components of any surveillance system (data quality, representativeness, and timeliness), we also faced many challenges. *Who is our audience?* We initially identified policymakers, providers, and the media as the potential audience of our surveillance system. Ongoing evaluation of actual usage will help us maintain an efficient and useful website. *What sources of data are available?* Pre-ESRD CKD is a non-reportable disease with low awareness, whose detection requires biologic data—excluding reliance upon questionnaire data alone. Additionally, the project was limited to passive surveillance, restricting prospective data collection. Thus, we have used a variety of existing, but unlinkable, data sources such as surveys (*e.g.*, NHANES), administrative data (*e.g.*, Veterans Affairs), and cohort studies to address many surveillance indicators. *What are the indicators of interest?* Because we wanted to address a variety of topics in CKD, such as burden, awareness, consequences, and quality of care, we used a modified Delphi process to prioritize >100 current indicators. However, as new areas of interest continue to emerge, we must evaluate and prioritize indicators for inclusion. In conclusion, our system continues to develop and evolve, but CKD surveillance remains a worthy and feasible goal, with the ability to report trends and the potential to direct public health research and programs.

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BREAST CANCER SCREENING IN AN ERA OF PERSONALIZED REGIMENS: A CONCEPTUAL MODEL FOR RISK- AND PREFERENCE-BASED SCREENING AT A POPULATION LEVEL. *Tracy Onega, Elisabeth Beaber, Emily Conant, Pamela Marcus, Brian Sprague (PROSPR Breast Cancer Working Group, Seattle WA 98109)

While there are proven benefits to breast cancer screening, recent studies have recognized the harms that are due in part to the current "one size fits all" approach to screening recommendations in the US. Updated conceptual frameworks are needed to guide the development of personalized screening approaches that maximize benefits and minimize harms for women. We developed a conceptual model emphasizing opportunities for personalization in breast cancer screening at the patient level across four key domains of care (screening awareness, detection, diagnosis, and treatment and survivorship). The model includes risk factors, patient preferences, new imaging modalities, and tumor characteristics as factors impacting personalized screening regimens. The patient perspective is embedded within multi-level systems of care, thus we also identified important process and outcome measures across the screening continuum. The Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) initiative by the National Cancer Institute is a unique setting for the development and evaluation of personalized strategies to refine the screening process and improve the risk-benefit ratio for individuals. The three PROSPR breast cancer screening research centers (University of Pennsylvania, University of Vermont, and Geisel School of Medicine at Dartmouth in conjunction with Brigham and Women's Hospital) are using this risk- and preference-based screening conceptual model to study personalized approaches across the screening continuum, such as using digital breast tomosynthesis, identifying novel prognostic markers for ductal carcinoma in situ, and improving care processes in primary care settings.

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THE TUBERCULOSIS INCIDENCE AMONG IMMIGRANTS IN DENMARK FROM 1992-2011 - IS IT TIME TO SCREEN? *Jan Wohlfahrt, Bolette Soborg, Mikael Andersson, Steen Ethelberg, Peter Andersen, Kaare Molbak (Dept of Epi Research, Dept of Infectious Disease Epi, Statens Serum Institut, Programme for Intervention Epi, ECDC, Copenhagen Denmark)

More than 60% of annual Danish tuberculosis (TB) cases are diagnosed among immigrants who contribute 8% of the Danish population. 60% of Danish immigrants derive from high TB incidence countries and two of the ten largest immigrant nationalities in 2011 were countries with high rates of multi-drug resistant TB. At present, no national TB screening of immigrants exist in Denmark. In this study the risk of TB among immigrants arriving in Denmark from 1992-2011 was estimated to assess whether post entry TB screening should be considered. The cohort was based on immigrants entering Denmark from 1992 to 2011 as identified in the Danish civil registration system (CRS). TB was identified by linkage with the Danish National Tuberculosis surveillance database using the unique CRS identifier. Time of entry and continent of origin were identified in the CRS and immigration status (data from 1997-2011) in the Danish Immigration Register, Ministry of Justice. Incidence rate ratios (RRs) were estimated by log-linear Poisson regression. 621.850 immigrants entered Denmark during the period. The median age was 23 years (Interquartile range; 19-29 years), 50% were male. A total of 2442 TB cases were identified. The overall TB incidence rate for the period were 607 per 100.000 person years for Sub- Saharan African immigrants and 124 per 100.000 for Asians. The incidence of TB was associated with time since entry (RR(first two year vs. >14 years in Denmark): 2.72 95% confidence interval (CI) 1.76-4.21), continent of origin (RR(Sub-Saharan Africans vs. EUEuropeans): 103 95% CI 77.3-139) and immigrant status (RR(asylum seekers vs. EU-applicants): 2.24). The study documents a high TB incidence among immigrants from high endemic countries. Implementing TB post entry screening could accelerate a decline in TB incidence and special attention should be given to asylum seeks and immigrants from high TB endemic countries.

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ASSESSMENT OF MEDICAL CLAIMS DATA FOR PUBLIC HEALTH REPORTING OF ENTERIC PATHOGENS COMMONLY TRANSMITTED BY FOOD. *Ellyn Marder, Anuradha Penaganti, Timothy Jones, John Dunn, Stephen Jones (Tennessee Department of Health, Nashville TN 37243)

An estimated 48 million foodborne illnesses occur in the US each year. Only about 5% of these illnesses are laboratory-confirmed. TDH conducts active surveillance for laboratory-confirmed cases of nine common foodborne pathogens as part of CDC's Foodborne Diseases Active Surveillance Network (FoodNet). We assessed medical claims data from Blue Cross Blue Shield of Tennessee (BCBST) members, which represent approximately 50% of the state population, to determine the feasibility of using medical claims data for public health reporting. ICD-9 codes were used to identify medical claims for FoodNet pathogens from BCBST administrative data from January 2003 to December 2011. A BCBST case was defined as a medical claim with a diagnosis code indicative of infection caused by a FoodNet pathogen. BCBST cases were matched to FoodNet cases, based on first name, last name, birthdate, sex, pathogen, and a difference of ≤60 days between claims date and specimen collection date. There were 6,739 BCBST cases and 37,654 FoodNet cases. Only 852 (13%) of the 6,739 BCBST cases were accounted for among FoodNet cases. Amongst BCBST cases, Yersinia, Salmonella, and Campylobacter were the most commonly matched pathogens to FoodNet cases, with 50%, 51%, and 52%, respectively. No Cyclospora, 1% of Vibrio, and 2% of E. coli BCBST cases matched FoodNet cases. The proportion of matched BCBST cases by pathogen was consistent with the proportion of FoodNet pathogens. BCBST cases include clinical diagnoses which may not necessarily be laboratory-confirmed; this may account for the larger number of BCBST cases. Potential reasons for the discrepant results include misdiagnosis and miscoding by medical providers and underreporting. Medical claims data have the potential to enhance population health surveillance. Further analyses are needed to refine the specificity of medical claims data for public health reporting and assess public health's capacity to receive and utilize such data.

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SOCIODEMOGRAPHIC CHARACTERISTICS AND SMOKING PATTERNS OF YOUNG ADULTS REACHED VIA A NATIONALLY REPRESENTATIVE CELL PHONE SAMPLE. *Sandra Echeverria, Cristine Delnevo, Daniel Gundersen, Cristine Delnevo (University of Medicine and Dentistry of New Jersey- School of Public Health, Piscataway NJ 07901)

A large segment of adults in the United States (US) live in cell phone-only homes that are increasingly difficult to reach via traditional landline Random Digit Dial (RDD) sampling. Moreover, research suggests that landline RDD surveys may bias certain prevalence estimates for subgroups such as younger adults and racially/ ethnically diverse populations. We present data on a nationally representative cell-phone RDD sample targeting racially and ethnically diverse young adults 18-34 years old. We examine who the sample reached by benchmarking sociodemographic characteristics of the sample to the 2010 US Census and the 2010 Behavioral Risk Factor Surveillance System (BRFSS). We also compared select smoking health indicators to the 2010 National Health Interview Survey. A total of 2,871 individuals were sampled representing over 59 million individuals, with an overall smoking prevalence of 24%. Unweighted, our survey was more similar to the Census than BRFSS for all demographics with the exception of Latinos. The mean absolute deviation was 3 percentage points for our survey vs. 7.1 percentage points for BRFSS. Results indicate comparable or better data quality as benchmarked against BRFSS, a well-known and widely used RDD public health survey. Moreover, these findings demonstrate the feasibility of reaching young adults via cell-phone sampling and suggest the need for continued integration of current telephone technologies to better reach all segments of the US population.

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SCREENING FOR PRECOCIOUS CERVICAL RIPENING TO PREDICT PRETERM DELIVERY: AN ASSESSMENT. *Qing Li, Nigel Paneth, Claudia Holzman, Louis Keith (Department of Epidemiology & Biostatistics, Michigan State University, East Lansing MI 48824)

Assessment of the cervix during the 2nd trimester has been used to predict risk of preterm delivery (PTD). Based on the criteria for screening and a theme issue on screening in Epidemiologic Reviews, precocious cervical ripening is a predisease and the target of a screening test. Our review aims to evaluate comprehensive cervical screening which assesses multiple dimensions of precocious cervical ripening. We searched PubMed, EMBASE, and Chinese electronic databases for large (n > 500) observational cohort studies of low-risk, pregnant populations. Ten data-sets (n = 22,050 pregnancies) described within 12 peer-reviewed articles met these criteria; most were from high-income countries. Hospitals in Finland, France, Hong Kong, Sweden, and UK included cervical assessment in routine prenatal care. Studies varied by gestational week cutoffs for PTD, timing, frequency, and mode of cervical assessment. Across six studies, ranges of sensitivity, specificity, and positive predictive value (PPV) of Bishop Score in digital examination were 20%-57%, 71%-99%, and 4%-38%. Seven studies reported transvaginal ultrasonography (TVS) measures of cervical length and cervical funneling, each along or combine. Ranges of sensitivity, specificity, and PPV of cervical length measure were 7%-49%, 87%-97%, and 6%-18%. Results of cervical funneling were 8%-33%, 92%-99%, and 3%-38%. Three studies reported greater specificity of cervical funneling than that for cervical length. Five of seven studies used both cervical length and funneling (either abnormal, or both abnormal) to create a composite measure which altered the above screening parameters. Methodological quality varied and only one study reported on inter-rater reliability. Comprehensive cervical assessment can predict PTD. Our review of current studies highlights the needs to develop better evidence-based protocols to determine the optimal parameters and usefulness of screening for precocious cervical ripening in pregnancy.

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EDUCATIONAL ATTAINMENT AND GESTATIONAL WEIGHT GAIN AMONG AMERICAN MOTHERS. *Alison Cohen, Chandni Kazi, David Rehkopf, Irene Headen, Barbara Abrams (University of California Berkeley School of Public Health, Berkeley CA 94720)

Gestational weight gain has implications for maternal and child health across the life course, but the majority of US women do not gain within the range recommended by the Institute of Medicine 2009 guidelines. Education is a major social determinant of health outcomes, but the relationship between educational attainment and gestational weight gain has not yet been conclusively established. Using the National Longitudinal Survey of Youth 1979 cohort, we use generalized estimating equations to calculate the association between educational attainment and gestational weight gain, controlling for a diverse array of social factors from across the life course and considering effect measure modification by race/ethnicity and pre-pregnancy overweight status. In general, women with more education are more likely to gain a recommended (as defined by 2009 Institute of Medicine guidelines) amount of gestational weight, and this finding is robust to sensitivity analyses and is independent of educational aspirations and educational expectations. For example, those who did not graduate from high school had a higher odds of inadequate gestational weight gain than high school graduates (odds ratio (OR): 1.34; 95% confidence interval (CI): 1.09, 1.64) and college graduates (OR: 2.06; 95% CI: 1.48, 2.87). Additionally, high school graduates had higher odds of inadequate gestational weight gain than college graduates (OR: 1.54; 95% CI: 1.17, 2.02). When we looked at excessive gestational weight gain as our outcome, among those who were not overweight at pre-pregnancy, women who graduated from high school had higher odds of excessive gestational weight gain than college graduates (OR: 1.37; 95% CI: 1.07, 1.74). To the best of our knowledge, this is the first study of the relationship between educational attainment and gestational weight gain to adjust for a wide range of potential confounders from across the life course.

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STATE-LEVEL INEQUALITY AND DEPRESSION AMONG A COHORT OF AMERICAN ADULTS. *Roman Pabayo, Ichiro Kawachi, Stephen Gilman (Harvard School of Public Health, Boston MA 02115)

Although cross-sectional and ecological studies have shown increased area-level income inequality is related to increased risk for depression, no longitudinal studies have been conducted. Therefore, the objective of this investigation is to examine the relationship between state-level income inequality and major depression among adults participating in a population-based, representative longitudinal study. We used data from the National Epidemiologic Survey on Alcohol and Related Conditions (n = 34,653). Respondents completed structured diagnostic interviews at baseline (2000-2001) and follow-up (2004-2005). State of residence was assigned a Gini coefficient, which is a measure of inequality. Weighted multi-level modeling was used to determine if US State inequality was a significant predictor of depression at baseline and at follow-up, while controlling for individual and state-level covariates. To determine if state inequality was associated with the incidence of depression, analysis was conducted excluding those who had a history of depression or at baseline. State-level inequality was associated with increased likelihood for depression among women only. In comparison to the lowest quintile of income inequality, there was increased risk for depression among women in the second [Odds Ratio (OR) = 1.17, 95% Confidence Interval (CI) = 0.85,1.61], third (OR = 1.22, 95% CI = 1.63), fourth (OR = 1.35, 95% CI = 1.02,1.80), and fifth (OR = 1.48, 95% CI = 1.13,1.94) quintiles at follow-up ($p < 0.05$ for the linear trend). We conclude that income inequality at the state level is a significant risk factor for the development of depression among women. These findings are consistent with prior evidence that women's status measured at the state level is associated with depression. Thus, state-level policies may be important to address for reducing the excess burden of depression among women.

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EFFECTS OF A HOUSING MOBILITY EXPERIMENT ON NEIGHBORHOOD QUALITY. *Quynh Nguyen, Nicole Schmidt, Eric Tchetgen, Maria Glymour, Joanna Almeida, Theresa L Osypuk (Northeastern University, Boston MA 02115)

Purpose: The Moving to Opportunity (MTO) trial is known to have influenced neighborhood poverty and select health outcomes, but the range of neighborhood characteristics, beyond poverty, influenced by MTO is not well documented. Methods: MTO was a randomized controlled trial in 5 US cities. Volunteer families were randomized (1994-1997) to public housing (in-place control group) or offered a voucher to subsidize private market rental apartments in any neighborhood (section 8 treatment group) or in low-poverty neighborhoods only (low-poverty treatment group). We analyzed 4-7 year follow-up survey data (in 2002) on neighborhood characteristics from adult and youth self-reports and interviewer-observed ratings. We also merged neighborhood data from the 2000 Census, public data sources, and 3 population-based surveys: Boston Neighborhood Survey, Project on Human Development in Chicago Neighborhoods, and New York Social Environment Survey. Using linear regression, we quantified the standardized effect of MTO on the residential environment. Results: We find that compared with controls, the low poverty and section 8 treatment arms had substantial improvements in externally-measured neighborhood economic conditions (0.6, 0.4 SD respectively), collective efficacy (0.5, 0.2 SD) and violent crime rates (-0.4, -0.3 SD), as well as moderate decreases in MTO participant-reported neighborhood disorder (-0.3, -0.2 SD). Differences relative to controls were larger for the low-poverty than for the section 8 group for neighborhood economic conditions and collective efficacy, but generally similar for violent crime and self-reported indicators of neighborhood disorder. Conclusion: Housing mobility programs account for 40% of US Department of Housing and Urban Development's budget. They can have positive and wide-ranging impacts on the residential environments of low-income families. Determining neighborhood characteristics important for health is a critical endeavor.

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PSYCHOMETRIC EVALUATION OF THE CHINESE VERSION OF THE SUBJECTIVE HAPPINESS SCALE. *Hairong Nan, Michael Y Ni, Paul H Lee, Wilson W.S Tam, Ying Ying Yu, Tai-Hing Lam, Gabriel M Leung, Ian McDowell (The University of Hong Kong, Hong Kong SAR China)

We validated a Chinese version of the 4-item Subjective Happiness Scale (SHS) by evaluating its correlations with physical and psychological health in the Hong Kong general population. The Chinese SHS was derived using forward-backward translation. A total of 6,030 Cantonese-speaking participants aged 15 and above years were recruited by random household sampling in 18 districts of Hong Kong. They completed the SHS, a single-item overall happiness scale, the Patient Health Questionnaire-9 (PHQ-9) and family APGAR scale. Among them, 203 underwent a re-testing of the SHS two weeks later. Respondents scoring in the 4th quartile of SHS were defined as "happy". Exploratory and confirmatory factor analyses supported a single factor with strong loadings for all 4 items. Cronbach's alpha was 0.82 and test-retest reliability was 0.69. The SHS correlated significantly with overall happiness (Rho = 0.56), perceived current (Rho = 0.32) and future health status (Rho = 0.22), family APGAR (Rho = 0.21), and PHQ-9 (Rho = -0.36) (all $p < 0.01$). We calculated multivariate adjusted odds ratios (and 95% confidence intervals) for happiness in relation to a range of variables, adjusting for age, sex, marital status and number of chronic conditions. The odds ratio for happiness relating to better perceived current health status was 1.51 (1.39-1.65); the odds ratio for future health status was 1.29 (1.16-1.42), while that for each increment in family APGAR score was 1.10 (1.08-1.13), and PHQ-9 score was 0.87 (0.84-0.90). Our data support the reliability and validity of the SHS as a brief measure of physical and psychological health-related happiness in a Chinese general population.

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ASSOCIATION OF ECONOMIC STRAIN WITH SUBJECTIVE ILL-BEING AMONG U.S. ADULTS: A TWO-LEVEL ANALYSIS. *Chaoyang Li, Guixiang Zhao, Xiao-Jun Wen, Lina Balluz, Satvinder Dhingra, Carol Crawford (Centers for Disease Control and Prevention, Atlanta GA 30333)

Life satisfaction is a measure of a person's subjective well-being. This measure attempts quantify information about the quality of a person's life. The financial crisis of 2007-2008 caused severe economic strain and potentially affected people's daily living. The objective of this study was to assess the association between economic strain measured by the economic stress index (ESI) and subjective ill-being (SIB) measured by life dissatisfaction among adults in the United States. Data from adults aged 18 years or older who participated in the 2009 Behavioral Risk Factor Surveillance System in the 283 counties were analyzed (n = 202,007). The ESI integrates unemployment rate, foreclosure rate, and bankruptcy rate at county level. Life satisfaction was measured by asking BRFSS participants the question "In general, how satisfied are you with your life?" Participants answered with one of the following: very satisfied, satisfied, dissatisfied, or very dissatisfied. SIB was defined as being "dissatisfied" or "very dissatisfied" with life. The hierarchical data were constructed by merging the county-level ESI data with the person-level BRFSS data and were analyzed with two-level log-linear models. In 2009, the mean ESI ranged from 4.3% to 21.4% with a median of 10.0% and the prevalence of SIB ranged from 1.2% to 11.1% with a median of 5.2% across the 283 counties. The mean ESI was significantly correlated with the prevalence of SIB at the county-level ($r = 0.3$, $p < 0.0001$). One percent increase in mean ESI was associated with about 4% higher prevalence of SIB (prevalence ratio [PR]: 1.04; 95% confidence interval [CI]: 1.03-1.05). The association remained statistically significant (PR: 1.02; 95% CI: 1.01-1.03) after adjusting for person-level demographic characteristics, socioeconomic status, health risk factors, and chronic diseases or conditions. In sum, economic strain was significantly associated with subjective ill-being among U.S. adults.

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LOW INCOME AND THE RISK OF HEART FAILURE. MEDIATION BY PHYSIOLOGICAL, PSYCHOLOGICAL AND BEHAVIORAL FACTORS. *Ingelise Andersen, Theis Lange, Finn Diderichsen, Eva Prescott, Naja Hulvej Rod (Department of Social Medicine, Institute of Public Health, University of Copenhagen, Copenhagen, Denmark, Copenhagen K Denmark)

Introduction: Low socioeconomic status is associated with risk of heart failure. We aimed to investigate the association between low equivalent income and first-time heart failure hospitalization and to calculate the expected mediated proportion of the physiological (fibrinogen, hypertension, hypercholesterolemia, diabetes and BMI), the behavioral (tobacco, alcohol, physical inactivity) and the psychological pathways (vital exhaustion), respectively. Material and Methods: Our analyses are based on 7,102 persons, aged 40-90 years, 57% women, from the Copenhagen City Heart Study (Denmark) 3rd wave taking place in 1991-3. Information on income and hospitalization was obtained from nationwide registries. During 18 years of follow-up 964 persons experienced first-time hospitalization with heart failure. The approach to measure the mediated proportion of the three potential pathways, were based on counterfactuals to calculate natural direct, indirect and total effects through each pathway by means of additive hazard models. Results: The total effect of being exposed to low income compared to high income increased the incidence of heart failure to 30.9 cases/10.000 person years (CI 95%: 8.5-53). Of these could 3.8 cases/ 10.000 person years (3.6-11.2) or 12% be attributed to a pathway through biomarkers. The mediated proportion was 13% for behavioral and 12% for psychological pathways. Analyses of the single covariates in the pathways indicate that physical inactivity, BMI $\geq$ 30kg/m2 and vital exhaustion have the strongest direct effect on heart failure. Conclusion: The results indicate that all three pathways contribute to the association between low income and the risk of heart failure. Additive hazards models calculate the actual number of cases associated with the different pathways, which might be intuitively easy to understand.

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LONGITUDINAL ASSOCIATIONS BETWEEN NEIGHBORHOOD RECREATIONAL FACILITIES AND CHANGE IN RECREATIONAL PHYSICAL ACTIVITY IN THE MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS. *Yamini Kesavan, Ana Diez-Roux, Kelly Evenson, Brisa Sanchez, Kari Moore (University of Michigan, Ann Arbor MI 48109)

Background: Many cross-sectional studies have investigated the relationship between neighborhood physical environment and physical activity. However, few studies have examined this relationship longitudinally, and no study has examined the association between change in objective measures of physical activity resources and change in physical activity in adults. Methods: We used longitudinal data from the Multi-Ethnic Study of Atherosclerosis on 6,814 adults aged 45-84 years at baseline. Physical activity was assessed via a semi-quantitative questionnaire at baseline and at two follow-up visits (approximately 1.6 and 3.2 years later). We measured the density of recreational facilities within 1 mile of each participant's home address and used linear mixed effects models to estimate the associations between change in recreational facility density and change in physical activity. Results: After adjusting for potential confounders, we found that a greater increase in recreational density was associated with a less pronounced decline in physical activity over time (mean difference in annual change in physical activity for each 1-unit increase in recreational density over time (95% confidence interval) = 10.3 (0.7, 19.9)). This association was stronger in older adults. Conclusion: Better access to recreational facilities may benefit middle-aged and older adults by enabling them to maintain activity levels as they age.

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VALIDATING THE FAMILY HARMONY SCALE IN HONG KONG CHINESE: JOCKEY CLUB FAMILY PROJECT. Paul H Lee, Ian McDowell, Richard Fielding, Sophia S. C Chan, Sunita M Stewart, Hairong Nan, Brandford H. Y Chan, *Michael Y Ni, Tai-hing Lam, Gabriel M Leung (University of Hong Kong, Department of Community Medicine / School of Public, Hong Kong SAR China)

Family harmony is a novel construct in health research that is particularly valued in Chinese culture, although there has not been a well validated instrument to date. Thus we developed the Family Harmony Scale (FHS), consisting of 24 items each describing a harmonious family in a holistic way and scored on a five-point Likert scale ranging from "strongly disagree" to "strongly agree". Its psychometric properties, convergent validity and discriminant validity were assessed based on a randomly chosen, representative sample of 17,807 Hong Kong Chinese participants. We found the scale to be internally consistent (Cronbach's alpha = 0.97) and stable over two weeks (test-retest reliability = 0.57). Confirmatory factor analysis showed that the theoretically-driven, full five-factor model (thematically labeled effective communication, conflict resolution, forbearance, identity, and quality time with family) yielded a good fit (Normed Fit Index = 0.95, Comparative Fit Index = 0.95, Standardized Root Mean Square Residual = 0.03), and the factor structure was invariant across sex and age. The FHS correlated with measures of family functioning, well-being, leisure time spent with family members, depressive symptoms, and with measures of emotional, but not physical symptoms. The FHS adds to other measures designed in the western context to measure family harmony in Chinese populations.

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RACIAL/ETHNIC AND GENDER DIFFERENCES IN ASSOCIATIONS OF SELF-REPORTED EXPERIENCES OF DISCRIMINATION WITH INFLAMMATION: THE MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS (MESA). *Kiarri Kershaw, Tene Lewis, Ana Diez Roux, Nancy Jenny, Kiang Liu, Frank Penedo, Mercedes Carnethon (Northwestern University Feinberg School of Medicine, Chicago IL 60611)

Chronic inflammation may link experiences of discrimination with increased cardiovascular disease risk, but few studies have examined this relationship. We assessed whether lifetime discrimination was associated with higher interleukin-6 (IL-6) and C-reactive protein (CRP) among Black, White, Asian, and Hispanic MESA participants ages 45-84 without a recent infection (n = 4,954). Lifetime discrimination was assessed by asking whether participants had ever been unfairly treated in 6 domains. Separate gender- and race/ethnicity-stratified linear regression models were used to assess associations of discrimination with log-transformed IL-6 and CRP. The prevalence of lifetime discrimination ranged from 17.1% in Asian women to 71.8% in Black men. White women who reported experiences of discrimination had 11.2% higher (95% confidence interval [CI]: 2.6%, 19.8%) IL-6 and 20.9% higher (95% CI: 5.3%, 36.5%) CRP than those who did not after adjusting for age, field center, education, income, current anti-inflammatory medication use, diabetes, and hypertension. Discrimination was also significantly associated with higher IL-6 (17.5%; 95% CI: 6.9%, 28.1%) and marginally associated with higher CRP (16.6%; 95% CI: -0.6%, 33.8%) among Hispanic men. Discrimination was unassociated with IL-6 among Black and Hispanic women, but it was significantly related to lower CRP in Black women and higher CRP in Hispanic women. Discrimination was marginally associated with higher IL-6 in Asian men ($p = 0.07$) but not CRP. All significant associations persisted after further adjusting for physical activity, current alcohol use, and current smoking; however associations attenuated for White and Hispanic women with adjustment for body mass index ($p < 0.10$). Discrimination was unassociated with IL-6 or CRP among Asian women, White men, and Black men. In summary, we found substantial variation in the relationship between discrimination and inflammation by race/ethnicity and gender.

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NEIGHBORHOOD SOCIAL PROCESSES AND OLDER ADULTS' SLEEP. *Jen-Hao Chen (University of Chicago, Chicago, IL 60637)

Good sleep is essential for health and wellbeing of older adults. Previous research has identified biological, behavioral, and socio-demographic factors that are associated with sleep duration and quality in older adults. Few studies that look beyond individual-level factors to considered the role of social environment. A large literature in medical sociology and social epidemiology has demonstrated the powerful effect of neighborhood social processes on health outcomes of older adults. However, relative few studies have examined whether and how neighborhood influence human sleep. This study contributes to this literature by investigating the association between neighborhood social processes and sleep in older adults using nationally representative data from the National Social Life, Health, and Aging Project (NSHAP). The NSHAP included 780 adults aged 62-91 in 2010-2011 with self-report sleep outcomes, actigraphhy data, and information of demographic characteristics and neighborhood processes. We focused on three dimensions of sleep outcomes: total sleep time, sleep timing, and sleep quality. Three neighborhood social processes were examined: perceived social interaction, perceived social trust, and perceived neighborhood disorder. Covariates included age, gender, race and ethnicity, education, marital status, household income, and household assets. Controlling for individual demographic characteristics and socioeconomic status, perceived social interaction and social trust within the neighborhood were not associated with any actigraphic sleep measures and self-report sleep outcomes. Perceived social disorder in neighborhood was associated with late bedtime and increased in self-report troubled sleep. Findings thus suggest that neighborhood social processes may not be an influential factor for older adults' sleep. However, living in disordered neighborhoods was associated with more sleep complaints and late bedtime suggesting that negative aspects of neighborhood social processes may lead older adults to overestimate their sleep problems.

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PERCEIVED DISCRIMINATION AND HEALTH: RESULTS FROM THE SURVEY OF THE HEALTH OF WISCONSIN (SHOW). *F Javier Nieto, Kristen C Malecki, Lynne M Morgan, Matthew C Walsh (Population Health Sciences, University of Wisconsin, Madison, Madison WI 53726)

Perception of discrimination has been associated with poor health but there is limited evidence regarding correlates and mediators of such relationships. In addition, many studies have focused solely on gender or racial discrimination. We used 2008-11 data from SHOW, an annual statewide probability sample of adults (n = 2,479, age 21-74 years) to examine the relation between perceived discrimination and both subjective and objective markers of health. Perceived lifetime discrimination was assessed using a modified version of the Jackson Heart Study questionnaire covering perception of discrimination based on age, gender, race, culture, physical appearance, religion, or sexual orientation. Cardiovascular health (CVH) was defined according to the American Heart Association definition, combining levels of seven risk markers (body mass index, cholesterol, glucose, diet, physical activity, blood pressure and smoking). About 42% of participants reported some lifetime discrimination. Perception of discrimination was more prevalent among males, minority, lower educated participants, but was not significantly different in urban compared to rural participants. Those reporting discrimination had higher prevalence of poor/fair health, poor CVH, depression, anxiety, obesity, smoking, food insecurity, lacked health insurance, had higher leukocyte count, lower FEV1. Compared to those perceiving no discrimination, the demographic and socioeconomic status-adjusted odds ratio (95% confidence interval) of poor CVH was 1.4 (1.0-2.1) and 1.8 (1.1-2.7) for those reporting rare and common instances of discrimination, respectively. This association become non-significant after further adjustment for psychosocial and behavioral correlates. Perceived discrimination is associated with a broad range of objective and subjective markers of health. Perception of discrimination might be a potential intermediary of psychosocial stress and both perceived and objective health.

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SUICIDAL BEHAVIOR BY BURNS AMONG WOMEN: THE SILENT SCREAM OF WOMEN IN IRAN. *Reza Alaghehbandan, Abdolaziz Rastegar Lari, Nicole A Dinn (Faculty of Medicine, Memorial University of Newfoundland, St. Johns NL Canada)

The aim of the study was to examine epidemiologic characteristics of suicidal behavior by burns among women in the two bordering provinces in Iran. A prospective population-based study of all suicidal behaviors by burns requiring hospitalization among women was conducted in the Iranian provinces of Khorasan (in border with Afghanistan) and Ilam (in border with Iraq) in 2006. These two bordering provinces suffered of years of war and economic instability with high rate of poverty and unemployment. Data were obtained from patients, family members, and/or significant others through interviews during the course of hospitalization. A total of 181 patients with suicidal behavior by burns requiring hospitalization were identified during the study period of whom 130 (71.8%) were female, representing an overall incidence rate of 9.0 per 100,000 person-year (P-Y). The incidence rate of suicidal behavior among women in rural areas was significantly higher than urban settings (18.2 vs. 5.9 per 100,000 P-Y respectively, $P < 0.001$). Median age of the patients was 23 years, with a mean (±SD) of 27.9 (±14.3) years. Approximately 70% of women were married and marital conflict was identified as the most common precipitating factor (94%). More than one third of women admitted to have been abused by family members (i.e. spouse, father-in-law), yet the remainder did not volunteer such information. Nearly 90% of the patients had an educational attainment level of high school or less. Median total body surface area burned (TBSA) was 70% with a mode of 100%. Mean TBSA among women who died was significantly higher than those who survived (87.8% vs. 41.8%, $P < 0.001$). Case fatality rate among this cohort was 52.3% (68/130). The high rate of suicidal behavior by burns among young, married women in rural areas in Iran is an alarming social tragedy. Despite international community's call on this, persistent conditions allow violence against women in Iran and these women continue to turn to the desperate remedy of self-burning. Findings of this study highlight the need for the implementation of a well-organized approach to reduce the incidence of suicide by burns among the most vulnerable populations in Iran.

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PUBIC HAIR REMOVAL AND VULVODYNIA. *Maheruh Khandker, Sarah Rydell, Bernard Harlow (University of Minnesota School of Public Health, Minneapolis MN 55454)

Removal of pubic hair has become increasingly common in the US and may contribute to inflammatory side effects. Vulvodynia, or chronic unexplained vulvar pain, is hypothesized to be a consequence of an altered immuno-inflammatory response. We sought to determine whether removal of pubic hair was associated with first onset vulvodynia. History of pubic hair removal was assessed in 99 women with clinically diagnosed vulvodynia and 67 randomly selected similarly aged controls residing in the Minneapolis-St. Paul Metropolitan area. Women self-reported the area(s) hair was removed and the method(s) used. Hair removal time frames assessed included: the first menstrual period to age 18, the year before onset of vulvar pain (reference year for frequency-matched controls), and within the last 3 months of survey completion. Virtually all cases and controls reported a history of some form of pubic hair removal. However, among women who removed pubic hair before the age of 18, those who removed hair from the entire mons pubis, genitals, and/or perineum had a 3-fold estimated risk of vulvodynia compared to those who removed hair from the bikini area, anus, and/or a portion of the mons pubis (95% Confidence Interval (CI): 1.2, 8.0). This association was attenuated the year before vulvodynia diagnosis (Odds Ratio = 2.3; 95% CI: 1.1, 5.0) and was non-significant 3 months prior to survey completion. Although more women reported shaving or waxing over other methods, there were no statistically significant associations in any of the age groups between the method of hair removal and vulvodynia. Our findings suggest that: a) the area in which hair is removed (the entire mons pubis, genital, and/or the perineum) and not the method of hair removal may contribute to the development of vulvodynia; and b) hair removed from the vulva earlier in life may trigger the development of vulvodynia during adulthood perhaps through a triggering of an altered immuno-inflammatory response.

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DEVELOPMENT, PROGRESSION, AND REMISSION OF LOWER URINARY TRACT SYMPTOMS ACROSS RACIAL/ETHNIC GROUPS: A POPULATION-BASED PROSPECTIVE STUDY. *Nancy Maserejian, Andre Araujo, Shan Chen, Gretchen Chiu, Carrie Wager, Varant Kupelian, John McKinlay (New England Research Institutes, Inc., Watertown MA 02472)

To examine the changing prevalence, progression and remission of LUTS, we conducted a population-based prospective study using a stratified 2-stage cluster random sample design. Men (N = 2,301) and women (N = 3,202) aged 30-79 y from Boston were recruited from 2002-2005. A 5-year follow-up visit was completed by 4,144 individuals (1,610 men; 2,534 women). LUTS was assessed by the American Urological Association Symptom Index (AUASI). For this analysis, we used improved weighting and missing data imputation methods: inverse probability weights were adjusted for non-response bias at follow-up, then post-stratified to the Boston census population; multiple imputation was based upon multivariate sequential regression. The prevalence of LUTS (AUASI > 8) increased slightly (19% baseline, 20% follow-up), but the subgroup reporting LUTS changed considerably over time. The percentage of men and women newly reporting LUTS was consistently 13% across black males, black females, Hispanic males, and white females. A lower percentage (7%) was observed in white males, while slightly more Hispanic females newly reported LUTS (15%). Most men with severe LUTS (AUASI > 20) at baseline reported severe LUTS at follow-up (61.5%). In contrast, 18.3% of women with severe symptoms at baseline continued to experience them at follow-up. Symptom remission was reported by 30-44%, most commonly among women and Hispanics. Worsening LUTS was reported by roughly one-fifth of white participants, one-fourth of black participants, one-fourth of Hispanic males, and one-third of Hispanic females. LUTS may be a chronic problem for only approximately half of the population with symptoms. Women's symptoms were more often dynamic (both improvement and worsening) compared to men's symptoms. Funded:U01DK56842 The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIDDK or the NIH.

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MALE MICROCHIMERISM AND SURVIVAL AMONG WOMEN. *Mads Kamper-Jørgensen, Anne-Marie Nybo Andersen, Henrik Hjalgrim, Vijayakrishna Gadi, Anne Tjønneland (University of Copenhagen, Copenhagen K Denmark)

Background: During pregnancy, a woman and her fetus exchange small quantities of cells and their persistence at later times is termed microchimerism. Microchimerism can substantially impact later maternal health. We studied the survival of women according to microchimerism status to elucidate whether this could be one reason why women benefit from parity compared with women who have never given birth and men. Methods: Male microchimerism status, measured as presence of Y chromosome in peripheral blood samples, was determined in 272 women from the large Danish Diet, Cancer and Health cohort when aged 50-64 years during 1993-1997. Women were followed up for cause-specific death in national Danish registers until end of 2009. Survival was analyzed using Cox regression. Results: Seventy percent (n = 190) of women were male microchimerism positive. During follow-up 21 women died, of which 10 (52%) were male microchimerism positive, and 10 were negative. Thirteen deaths (62%) were due to cancer, 5 (24%) were due to cardiovascular disease, and 3 were due to other causes. Male microchimerism presence was associated with a significantly reduced relative risk of all-cause mortality of 0.39 (95% confidence interval 0.16-0.95). The relative risk of death from cancer and cardiovascular disease was 0.24 (95% confidence interval 0.08-0.76) and 1.40 (95% confidence interval 0.15-13.05), respectively, among male microchimerism positive compared with negative women. Conclusions: Although the biologic mechanisms are not precisely known, male microchimerism presence in peripheral blood of women is associated with substantial beneficial impact on women's survival. The results also indicate that the role of male microchimerism may vary for different diseases.

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THE ASSOCIATION OF REPRODUCTIVE AND LIFESTYLE FACTORS WITH A SCORE OF MULTIPLE SEX HORMONES. *Amy L Shafrir, Xuehong Zhang, Elizabeth M Poole, Susan E Hankinson, Shelley S Tworoger (Harvard School of Public Health, Boston MA 02115)

Associations between individual sex hormones and reproductive and lifestyle factors have been investigated; however, limited research has explored the relationship between these factors and multiple hormones simultaneously. We recently reported that having high levels of multiple sex hormones increases the risk of breast cancer among postmenopausal women, suggesting that understanding the determinants of high levels of multiple sex hormones is important. This analysis included 1,175 postmenopausal women from the Nurses' Health Study who provided blood samples in 1990, were not current postmenopausal hormone users at blood draw, and were included as controls in the breast cancer nested case-control study described above. A hormone score was created by summing the number of hormones each woman had above (or below for sex hormone binding globulin) the age-adjusted geometric mean, considering estrone, estradiol, estrone sulfate, testosterone, androstenedione, dehydroepiandrosterone sulfate, prolactin and sex hormone binding globulin. Body mass index (BMI) was positively associated with the hormone score with a 19% (95% confidence interval: 15%, 24%) increase in the score per 5 unit increase in BMI ($p < 0.0001$). Additionally, women with a history of benign breast disease (BBD) had an 8.4% (95% CI: 0.59%, 15%) lower hormone score compared to women without a history of BBD ($p = 0.036$). Duration of past postmenopausal hormone use, family history of breast cancer, parity, physical activity and smoking status were not associated with the hormone score. Overall, traditional risk factors for breast cancer were not associated with having high levels of multiple sex hormones, with the exception of BMI and history of BBD. Analyses also will be conducted examining other reproductive and hormonal factors including age at first birth and duration of breastfeeding. Additionally, an expanded definition of the hormone score using deciles of hormone levels will be evaluated.

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BLOOD MERCURY LEVELS IN PREGNANT AND NON-PREGNANT WOMEN IN THE UNITED STATES (NHANES 1999-2010). *Hilda Razzaghi, Sarah Tinker, Krista Crider (Centers For Disease Control and Prevention, Atlanta GA 30033)

Background: Prenatal exposure to methyl mercury is associated with adverse neurological development in children. We examined total blood mercury (BHg) levels and predictors of higher BHg levels in pregnant and non-pregnant women. Methods: Data from 1,183 pregnant women aged 16-49 years from the 1999-2006 National Health and Nutrition Examination Survey (NHANES), and 7,844 non-pregnant women aged 16-49 years from the 1999-2010 NHANES were analyzed. We estimated geometric mean BHg levels, as well as characteristics associated with higher mercury levels (≥3.5 μg/L) in crude and adjusted models. Results: After adjusting for age (16-25, 26-35, and 36-49) and race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, and other/multiracial), geometric mean BHg levels were similar for pregnant women (0.81 μg/L, 95% confidence interval [CI]: 0.71, 0.91) and non-pregnant women of childbearing age (0.92 μg/L, 95% CI: 0.82, 1.03). Characteristics associated with higher mercury levels were similar for pregnant and non-pregnant women: older age (35+ years), higher education, and higher poverty income ratio. The most significant predictor of high BHg levels for both groups was any seafood consumption in the last 30 days (Odds ratio [OR]: 20.2, 95% CI: 5.29, 77.2; OR: 17.3, 95% CI: 8.98, 33.5, respectively). Conclusion: Pregnancy status does not appear to be strongly associated with BHg levels in women of childbearing age; among both groups seafood consumption is the strongest predictor of high BHg.

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COMPARABLE ASSOCIATIONS OF CARDIOVASCULAR RISK FACTORS MEASURED IN EARLY ADULTHOOD AND AGAIN IN MIDDLE-AGE WITH CAROTID INTIMA-MEDIA THICKNESS IN MIDDLE-AGED WOMEN: THE AVON LONGITUDINAL STUDY OF PARENTS AND CHILDREN (ALSPAC). *Abigail Fraser, Corrie Macdonald-Wallis, Debbie Lawlor (University of Bristol, Bristol UK)

Background: Early adulthood is a 'missing link' in the lifecourse epidemiology of cardiovascular disease (CVD), with few studies looking earlier than menopause for causes of female CVD. Aims: 1. To study cross-sectional associations of CVD risk factors (age, smoking, adiposity, blood pressure (BP), diabetes, fasting lipids, insulin, and glucose) with carotid intima-media thickness (cIMT) in women in middle age. 2. To compare associations of age, smoking, adiposity, BP, and diabetes assessed in early adulthood and again in middle age with cIMT in middle-age. 3. To quantify the difference in cIMT related to change in body mass index (BMI) and BP in adulthood. Setting and Methods: UK, population based prospective pregnancy cohort. 4500 women had CVD risk factors and cIMT measured at a mean age of 48 (4.4) years (middle age). 3500 of these women also had information on CVD risk factors measured 20 years earlier at a mean age of 29.6 (4.5) years (early adulthood). We used a multilevel model to quantify the associations of change in BMI and in BP between early adulthood and middle age with cIMT. Results: Mean cIMT was 0.56mm (0.06). Associations between CVD risk factors in early adulthood and in middle age and cIMT were comparable. For example, a 1SD greater BMI measured in early adulthood was associated with a 0.004mm (0.002, 0.006) greater cIMT compared to 0.003mm (95% CI: 0.001, 0.005) for middle age; a 1SD increase in SBP in early adulthood was associated with a 0.006mm (0.004, 0.007) greater cIMT compared to 0.010mm (95% CI: 0.009, 0.012) for middle age. A 1mmHG increase in SBP change per year was associated with a median increase of 0.017mm in cIMT (2.5-97.5 centiles: 0.009, 0.031). Conclusions: Readily available information collected early in the life course can be used to identify women who are at increased risk of CVD later in life. Assessing risk at this time (i.e. during the reproductive years) could be useful as women may be particularly open to lifestyle changes during these years.

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SELF REPORTED HISTORY OF KELOIDS IS NOT ASSOCIATED WITH PREVALENT FIBROIDS IN YOUNG AFRICAN AMERICAN WOMEN. *Quaker Harmon, Donna Baird (National Institute of Environmental Health Sciences, Research Triangle Park NC 27709)

Study Design: The Study of Environment, Life-style, & Fibroids (SELF), is a volunteer cohort of over 1600 African American women aged 23-34 years from the Detroit, Michigan area. Enrollment began in November, 2010 and ended in December, 2012. Data are available for the first 1196 women. Participants self-reported raised (hypertrophic) scars and scars extending beyond the limits of the original injury (keloid) during a telephone interview conducted by trained research staff. Participants also received a study related ultrasound examination to identify prevalent fibroids. Log linear regression was used to model the association between abnormal scars and prevalent fibroids, controlling for possible covariates. Specific characteristics of fibroids (location, number, size) were also examined with respect to scar type using chi-square and ANOVA. Results: Keloids (9.0%), hypertrophic scars (28%), and fibroids (23.8%) were all common in this cohort. There was no association between scaring and fibroids [adjusted Risk Ratio, RR (95% Confidence Interval, CI): 0.7 (0.5-1.1) for keloids and 0.9 (0.8-1.2) for hypertrophic scars]. Nor was there any indication of an association between specific fibroid characteristics and scaring. Conclusion: Despite some biological similarities between fibroids and abnormal scars, African American women with one of these conditions were no more likely than would be expected by chance to have the other condition.

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USE OF TANNING BEDS, SUN EXPOSURE AND THE INCIDENCE OF ENDOMETRIOSIS. *Marina Kvaskoff, Jiali Han, Stacey Missmer (Channing Division of Network Medicine, Brigham & Women's Hospital and Harvard Medical School, Boston MA 02115)

An association between endometriosis and cutaneous melanoma has been reported, and evidence suggests that these diseases may share constitutional risk factors. Since exposure to ultraviolet radiation (UVR) is the major environmental risk factor for melanoma, our objective was to explore its relation to endometriosis risk. We prospectively analyzed data from the Nurses' Health Study II, a cohort of 116,678 female US nurses aged 25-42 years at enrollment in 1989 with follow-up for >20 years since. We used Cox proportional hazards regression models to calculate multivariable relative risks (RR) and 95% confidence intervals (CI). During 621,742 woman-years of follow-up, 4705 cases of laparoscopically-confirmed endometriosis were reported among premenopausal Caucasian women. Tanning bed use during high school through age 35 was associated with significantly increased endometriosis risk as frequency and age of exposure increased (compared with never tanning bed exposure; <2 times/year at any age: RR = 1.01; ≥3 times/year in high school/college only: RR = 1.05; ≥3 times/year at 25-35 years only: RR = 1.17; ≥3 times/year both age periods: RR = 1.27; P_{trend} = 0.0002). Endometriosis risk was increased linearly with higher number of sunburns at ages 15-20 years (P_{trend} = 0.05) and percentage of time using sunscreen in summer (P_{trend} = 0.02). In contrast, risk was decreased with UVB flux in state of birth (P_{trend} = 0.04), in state lived most at age 15 years (P_{trend} = 0.01) and in state lived most at age 30 years (P_{trend} = 0.0002). These results suggest that intense artificial or recreational UVR exposure increases endometriosis risk, whereas ambient sunlight UVR exposure decreases risk. These novel findings need to be confirmed in other populations, and more research is needed to understand their underlying mechanisms.

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LATITUDE AND ULTRAVIOLET RADIATION DOSE IN BIRTHPLACE IN RELATION TO MENARCHEAL AGE IN A LARGE VOHORT OF FRENCH WOMEN. *Marina Kvaskoff, Laure Dossus, Anne Bijon, Pierre Engel, Jean Verdebout, Beatrice Fervers, Marie-Christine Boutron-Ruault, Francoise Clavel-Chapelon, Sylvie Mesrine (Inserm U1018, Centre for Research in Epidemiology and Population Health (CESP), Gustave Roussy Institute, Team 9, Villejuif - France)

Age at menarche is an important determinant of hormonal-related neoplasia and other chronic diseases. Spatial and temporal variations have been observed in industrialized countries; in particular, ecological studies suggest a North-to-South gradient in menarcheal age across several countries of the Northern hemisphere. However, the mechanisms underlying this association are unclear. Although a role of ultraviolet radiation (UVR) may be speculated, no previous investigation explored its relation to timing of menarche. We examined geographic variations in self-reported age at menarche and explored the effects of both latitude and UVR dose on the onset of menarche in 88,278 women from the French E3N prospective cohort, aged 40-65 years at inclusion in 1990. The mean age at menarche was 12.8 years. After adjustment for potential confounders (birth cohort, prematurity, birth weight and length, father's income index, body shape in childhood, food deprivation during World War II, population of birth place, number of siblings, breastfeeding exposure, and indoor exposure to passive smoking during childhood), latitude and UVR dose (annual or spring/summer) in county of birth were significantly associated with age at menarche (P for trend <0.0001). Women born at lower latitudes, or in regions with higher annual or spring/summer UVR dose, had a 3 to 4-month earlier menarche than those born at higher latitudes or in regions with lower UVR. On a continuous scale, a 1 degree increment in latitude resulted in a 0.04-year older age at menarche (95% CI: 0.03; 0.05), while a 1 kJ/m^2 increment in annual UVR dose resulted in a 0.42-year younger age at menarche (95% CI: -0.55; -0.29). These data suggest that sunlight exposure in childhood may influence sexual maturation in women.

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AGE AT NATURAL MENOPAUSE IN RELATION TO ALL-CAUSE AND CAUSE-SPECIFIC MORTALITY IN A FOLLOW-UP STUDY OF U.S. BLACK WOMEN. *Se Li, Lynn Rosenberg, Lauren Wise, Deborah Boggs, Michael LaValley, Julie Palmer (Slone Epidemiology Center, Boston University, Boston MA 02215)

Objectives: Early age at natural menopause has been associated with increased all-cause mortality in several studies, although the literature is not consistent. This relation has not been examined among African American women. Study design: We assessed the relation of age at natural menopause to all-cause and cause-specific mortality in the Black Women's Health study: 59,000 African-American women were enrolled in 1995 and were followed for deaths through 2008. At baseline and biennially, participants reported on reproductive and medical history, including gynecologic surgeries and exogenous hormone use. Mortality data were obtained from the National Death Index. Multivariable Cox proportional hazard models were used to estimate mortality rate ratios (MRR) and 95% confidence intervals (CI) among the 11,212 participants who experienced a natural menopause. Results: Of 692 deaths identified during 91,954 person years of follow-up, 261 were due to cancer, 199 to cardiovascular diseases and 232 to other causes. Early natural menopause was associated with increased all-cause mortality (MRR = 1.34, 95% CI 0.96-1.84 for age at menopause <40 vs. 50-54 years; P-trend = 0.04) and with the subcategories of death considered–cancer, cardiovascular disease, and all other causes. The associations were stronger among never users of postmenopausal female hormones. Conclusions: In this large prospective cohort of African-American women, early natural menopause was associated with a higher rate of all-cause and cause-specific mortality. These findings provide support for the theory that early natural menopause may be a marker of accelerated somatic aging.

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CHILDBEARING FACTORS IN RELATION TO ALL-CAUSE AND CAUSE-SPECIFIC MORTALITY IN A FOLLOW-UP STUDY OF U.S. BLACK WOMEN. *Se Li, Lynn Rosenberg, Lauren Wise, Julie Palmer (Slone Epidemiology Center, Boston University, Boston MA 02215)

Background: There has been a long-term debate about whether reproductive history influences mortality later in life. Previous studies have been inconclusive. Methods: We prospectively investigated the relation of parity, age at first birth, age at last birth, and lactation to all-cause and cause-specific mortality. We followed 57,757 U.S. black women aged 21-69 years at enrollment in the Black Women's Health Study (BWHS) from 1995 to 2008. Multivariable Cox proportional hazard models were used to estimate mortality rate ratios (MRR) and 95% confidence intervals (CI). Results: Of the 2,455 deaths identified during 716,580 person years of follow-up, 922 were due to cancer, 618 to cardiovascular diseases, and 915 to other causes. Among women under age 55, high parity was associated with increased all-cause mortality (MRR = 1.65, 95% CI 1.25-2.18, for parity ≥4 vs. 1, P-trend < 0.001), with a 53% increase in cancer mortality and a 131% increase in cardiovascular mortality; late age at last birth was associated with lower all-cause mortality (MRR = 0.63, 95% CI 0.46-0.87, for last birth at age ≥35 vs. <25 years, P-trend = 0.01), with a 41% decrease in cardiovascular mortality and 33% decrease in other-cause mortality. In contrast, among women ≥55 years, neither parity nor age at first birth was associated with all-cause or cause-specific mortality. Conclusions: Our data support the hypothesis that somatic resources used for reproduction may compete with resources required for longevity. Among parous women, late age at last birth may be a marker of reduced reproductive or somatic aging. For women who survive beyond 55 years, the impact of reproductive history on all-cause or cause-specific mortality is negligible.

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CADMIUM, LEAD AND MERCURY EXPOSURE AND PARAOXONASE 1 (PON1) ACTIVITY IN WOMEN. *Anna Pollack, Lindsey Sjaarda, Katherine Ahrens, Sunni Mumford, Rick Browne, Neil Perkins, Jean Wactawski-Wende, Enrique Schisterman (Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda MD 20892)

Paraoxonase 1 (PON1), a key antioxidant enzyme related to cardiovascular health, may be impaired by exposure to metals. We evaluated the relationship between blood metal levels and PON1 activity in 250 healthy, premenopausal women followed for ≤ 2 menstrual cycles using data from the BioCycle Study (2005-2007). Cadmium, lead and mercury levels were measured using blood samples collected for this purpose at baseline. PON1 arylesterase and paraoxonase activities were measured ≤8 times during each cycle. Linear mixed models were used to estimate the effects of low, medium and high tertiles of cadmium, lead, and mercury concentrations, respectively, on arylesterase and paraoxonase activity. All analyses were stratified by PON1 QI92R gene polymorphism (QQ wild type homozygous, n = 99; QR heterozygous, n = 117; RR homozygous mutant, n = 34), due to the known interaction between genotype and PON1 enzyme activity, and were adjusted for age, race, body mass index, smoking and dietary intake (as relevant for each metal). Arylesterase activity was lower in the middle cadmium tertile compared with the lowest tertile among women with QR (-15.2%: 95% confidence interval [CI] -23.0 to -6.8) and RR (-25.7%: CI -42.7 to -3.7) genotypes. Similarly, among RR women, those within the high and medium lead tertiles had lower arylesterase activity compared with the lowest tertile (-24.9%: CI -44.2 to 0.8 and -27.7%: CI -45.1 to -5.0, respectively). Paraoxonase activity was also lower in the medium compared with the lowest cadmium tertile (-30.4%: CI -48.0 to -6.9) among the RR genotype and was lower in the medium compared with the lowest tertile for mercury (-25.5%: CI -38.7 to -9.3) among the QQ genotype. Our findings suggest that blood metal levels are associated with decreased PON1 functional activity in women, and these effects vary by PON1 genotype.

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ACCESS TO PRIMARY CARE PROVIDER AND ADHERENCE TO MAMMOGRAPHY SCREENING. *Alyssa Kick, *Balakrupa Ramachandran, Margaret Gates (University at Albany School of Public Health, Rensselaer NY 12144)

Background: Many women fail to utilize screening mammography despite its proven effectiveness in the early detection of breast cancer. Factors associated with access to comprehensive healthcare services may hinder the ability of a woman to obtain a regular mammography. This study assessed the relationship between having a regular primary care provider (PCP) and adherence to recommended mammography screening guidelines in New York State women between ages 50 and 74. Methods: The study used data obtained from the 2010 New York State administration of the Behavioral Risk Factor Surveillance System telephone survey. Analysis was restricted to women between the ages of 50 and 74 as per breast cancer screening recommendations issued by the US Preventive Services Task Force. Women who did not obtain a mammography within the last two years were classified as cases (n = 375) whereas women who obtained a mammography within the last two years were classified as controls (n = 2125). Multivariable logistic regression was used to estimate odds ratios and 95% confidence intervals (CI) for the association of PCP status and related healthcare access exposures with adherence to recommended mammography screening guidelines after adjusting for healthcare access covariates, income and age. Results: The odds of not following the recommended mammography screening guidelines were 2.22 times greater among women who did not have a PCP as compared to women who did [95% CI: 1.35, 3.64]. Routine checkups, the cost of medical care, and income were also found to be important predictors of adherence to recommended mammography screening guidelines. There was no evidence of variation in the results by race, ethnicity or education. Conclusions: Primary care provider status was found to be an important determinant of adherence to recommended mammography screening guidelines for women in New York State. The expansion of healthcare access could improve utilization of preventative health services.

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EPIDEMIOLOGIC AND MEDICAL FACTORS ASSOCIATED WITH ANTIBODIES AGAINST TUMOR ASSOCIATED ANTIGENS MUC1 AND MUC16: POSSIBLE RELEVANCE TO OVARIAN CANCER. *Kristina Williams, Allison Vitonis, Hidemi Yamamoto, Raina N Fichorova, Daniel Cramer (OB/GYN Epidemiology Center, Brigham and Women's Hospital, Harvard Medical School, Boston MA 02115)

MUC1 (CA15.3) and MUC16 (CA125) are important glycoproteins involved in cell protection and immune signaling and are overexpressed in neoplastic and inflammatory conditions. We have proposed that various events lead to MUC1 expression and cause either enhanced immune surveillance or immune tolerance of ovarian cancer. The level of anti-MUC1 antibodies may be a biomarker of risk in this model. We sought to determine whether anti-MUC16 antibodies also exist and what factors determine their presence. We used a reverse capture assay to measure IgG antibodies against both MUC1 and MUC16 in 200 healthy women and identified epidemiologic variables affecting each. Variables affecting either anti-MUC1 or anti-MUC16 antibodies included BMI, smoking, parity, history of mastitis, endometriosis, history of bladder infections, estimated ovulatory cycles, and hysterectomy. In an age-adjusted model, variables associated with a higher level of anti-MUC1 antibodies included fewer pack-years of smoking ($p < 0.0001$), BMI < 25, history of mastitis ($p = 0.009$), fewer ovulatory cycles, history of bladder infections ($p = 0.03$), and hysterectomy ($p = 0.03$). In a similar model, variables associated with higher level of anti-MUC16 antibodies included fewer pack years of smoking ($p = 0.0004$), fewer ovulatory cycles, mastitis ($p = 0.02$), and bladder infections ($p = 0.03$). Anti-MUC16 antibodies were also higher in parous than nulliparous ($p = 0.02$), parity >3 than parity 1-2 ($p = 0.02$), and in women without endometriosis. These results suggest that, like anti-MUC1 antibodies, levels of anti-MUC16 antibodies correlate with various risk factors for ovarian cancer and may provide a common framework for biologic mechanisms that underlie the association between these risk factors and cancer. Future studies of mucin antibodies and their interaction with epidemiologic factors in larger populations of cancer cases and controls are warranted.

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HEALTH RELATED BEHAVIOURS AMONG MOTHERS OF PRESCHOOL CHILDREN. *Yasser Sabr, Sarka Lisonkova, K S Joseph (University of British Columbia, Vancouver BC Canada)

Objective: To examine the effect of younger versus older children in the family (ages <6 vs. 6-11 years) on the mother's physical activity, and smoking status. Methods: We studied all women who participated in the Canadian Community Health Survey (CCHS), 2009-2010, were 18–59 years old and had at least one child aged <11 years. The CCHS is a multi-stage health survey involving 124,188 respondents who form a representative sample of the Canadian population. Mothers with at least one child aged <6 years were contrasted with mothers with at least one child aged 6-11 years but no younger children. The association with low physical activity (<15 minutes/day), and smoking (occasional or regular vs. none) was quantified using odds ratios (OR) and 95% confidence intervals (CI). Logistic regression was used to adjust for maternal age, marital status, education, household size, income, and employment status. Results: Among 11,380 women in the study, 65.4% had younger children, 63.1% had low physical activity and 23.7% smoked. The odds of low physical activity were 1.25 times greater among mothers of younger vs. older children (adjusted OR = 1.25, 95% CI 1.15-1.37). In contrast, the odds of smoking were lower among mothers of younger children, as compared with those who had older children (adjusted OR = 0.77, 95% CI0.69-0.86). Conclusions: Mothers of young children were less likely to smoke; however, they were more likely to be less physical active. Support and effective strategies are required to help mothers with young children increase their physical activity.

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CORRELATION OF URINE AND PLASMA CYTOKINE LEVELS AMONG REPRODUCTIVE AGED WOMEN. *Carrie Nobles, Elizabeth Bertone-Johnson, Alayne Ronnenberg, Joycelyn Faraj, Sofija Zagarins, Biki Takashima-Uebelhoer, Brian Whitcomb (University of Massachusetts Amherst, Amherst MA 01003)

Measurement of circulating cytokines in serum or plasma samples is important in many areas of health research. However, measuring cytokine levels in urine may be more practical as it can be collected and stored at home, has lower cost and processing time, and reduced participant burden. We assessed the correlation of urine and plasma cytokine levels in matched samples from healthy reproductive-aged women ($n = 61$) in the UMass Vitamin D Status Study (2006-2009). Mid-luteal phase samples were obtained during a single visit by trained staff. Cytokines evaluated include interleukin (IL)1β, IL2, IL4, IL5, IL6, IL7, IL8, IL10, IL12p70, IL13, tumor necrosis factor-alpha (TNFα), granulocyte macrophage colony stimulating factor (GMCSF) and interferon-gamma (IFNg). The overall proportion of cytokine measures below the limit of quantification was 4.7% for plasma and 17.3% for urine. Samples below the limit of quantification were set to a standard value and urine measures were adjusted for creatinine. Pearson correlation coefficients were used to evaluate the association between log-transformed cytokine levels in plasma and urine. Estimated correlation coefficients for plasma and urine cytokine levels were: IL1β ($r = 0.001$, $p = 0.99$), IL2 ($r = -0.21$, $p = 0.10$), IL4 ($r = -0.28$, $p = 0.03$), IL5 ($r = -0.07$, $p = 0.57$), IL6 ($r = -0.07$, $p = 0.58$), IL7 ($r = 0.01$, $p = 0.92$), IL8 ($r = -0.20$, $p = 0.13$), IL10 ($r = 0.06$, $p = 0.67$), IL12p70 ($r = 0.02$, $p = 0.87$), IL13 ($r = 0.04$, $p = 0.73$), TNFα ($r = -0.18$, $p = 0.17$), GMCSF ($r = -0.08$, $p = 0.55$) and IFNg ($r = 0.09$, $p = 0.51$). Lack of correlation of plasma and urine cytokine levels may be related to low levels of circulating cytokines in the study population. Results suggest that cytokine levels in urine may not be a good proxy for those in plasma in populations with low levels of inflammation.

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THE RELATIONSHIP BETWEEN WIDOWHOOD AND PHYSICAL AND MENTAL HEALTH: RESULTS FROM A NATIONALLY REPRESENTATIVE SAMPLE OF OLDER ADULTS. *Anusha Vable, M Maria Glymour, SV Subramanian (Harvard School of Public Health, Boston MA 02115)

Background: The increase in mortality following spousal bereavement ("the widowhood effect") is well documented, however little is known regarding changes to physical or mental health that precede spousal death. This paper seeks to elucidate the effect of spousal bereavement on mobility and mental health markers. Methods: Participants in the Health and Retirement Study ($n = 9045$) who were either continuously married or widowed between 2004 and 2010 and with outcome assessments in 2006, were classified into the following exposure categories: a) 7,826 "continuously married" b) 430 "widowed" (became widowed between 2004 and 2006, prior to outcome assessments), and c) 386 "pre-widowed" (became widowed between 2006 and 2008, after outcome assessments). Linear regression models predicting functional mobility, gross motor skills, and number of anxious/depressive symptoms were adjusted for age, race, gender, education, childhood SES, birth place, income, wealth, self-reported health, and number of health conditions. Results: Compared to the continuously married, widowed individuals had higher anxious/depressive symptoms (1.35, 95% Confidence Interval (CI): [1.18, 1.51]); pre-widowed individuals also had elevated anxious and depressive symptoms compared to the continuously married (0.41, 95% CI: [0.24, 0.58]), but the difference was smaller. Widowed individuals had similar mobility (0.08 additional units, $p = 0.143$), but worse gross motor skills (0.08, $p < 0.024$) than the continuously married; among the pre-widowed, however, both the mobility (0.19, $p = 0.001$) and gross motor skills (0.13, $p = 0.001$) were worse compared to married individuals. Conclusions: Elevations in depressive symptoms are evident even before widowhood, suggesting that part of the "widowhood effect" might be attributable to experiences that preceded widowhood, such as care giving or grief associated with spousal illness.

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OBESITY AND LIFE EXPECTANCY AMONG LONG LIVED BLACK ADULTS. *Pramil Singh, Patti Herring, Gary Fraser, Joan Sabate (Center for Health Research, Loma Linda University, Loma Linda CA 92354)

Background. In samples of African Americans and the elderly, obesity is often not found to be risk factor for mortality. These data contradict the evidence linking obesity to chronic disease in these groups. Our objective was to determine whether obesity remains a risk factor for mortality among long lived Black adults. Methods. The Adventist Health Study 2 (AHS-2) is a large prospective cohort study of Seventh-day Adventist church members who are encouraged by faith-based principles to avoid tobacco, alcohol, and meat consumption. We conducted an attained age survival analysis of 22,884 US Blacks of the cohort-half of whom attained an age of 58 to 108 years during the follow-up (adult life expectancy of 84 years in men, 89 years in women). Results. Women in the highest BMI quintile (>33.8) experienced a significant 61% increase (hazard ratio [95% CI] =1.62 [1.23, 2.11] relative to the middle quintile) in mortality risk and a 6.2 year [95% CI 2.8 to 10.2 years] decrease in life expectancy. Men in the highest BMI quintile (>30.8) experienced a significant 87% increase (hazard ratio [95% CI] = 1.87 [1.28, 2.73] relative to the middle quintile) in mortality risk and 5.9 year [95% CI 2.1 to 9.5 years] decrease in life expectancy. Obesity (>30) was a significant risk factor relative to normal weight (18.5 to 24.9) in never-smokers. Instantaneous hazards indicated excess risk from obesity was evident through at least age 85 years. The non-obese tended to follow plant-based diets and exercise vigorously. Conclusion. Avoiding obesity promotes gains in life expectancy through at least the eighth decade of life in Black adults. Evidence for weight control through plant-based diets and active living was found in long-lived non-obese Blacks.

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MEMORY FUNCTIONING AND 2-YEAR MORTALITY RISK: COMPARING CONVENTIONAL AND GENETIC INSTRUMENTAL VARIABLE ESTIMATES. *Jessica Daniel, Stefan Walter, Paola Gilsanz, Ichiro Kawachi, M Maria Glymour (Harvard University School of Public Health, Boston MA 02115)

Background: Memory declines often presage death, but it is unclear if memory decline increases mortality risk directly or is a consequence of underlying illnesses that lead to death. We estimated the effect of memory functioning on mortality risk using a conventional model and a polygenic risk score as an instrumental variable (IV) for memory impairment. Methods: Health and Retirement Study participants (n = 12,123) provided genetic data in either 2006 or 2008. We created a genetic IV for memory impairment based on 10 loci identified as genome-wide significant predictors of dementia in the AlzGene database (range 0.38-5.05). The instrumented phenotype was a previously validated composite memory score, assessed the year the participant provided genetic data. Mortality was defined as death before the next interview wave (~2 years). We used linear regression models to estimate conventional risk differences (RD) for mortality associated with a 1 standard deviation (SD) difference in memory. We used two stage least squares regression to derive the IV estimate of the RD for memory on mortality within two years, restricting to non-Hispanic whites and controlling for age, sex, and population stratification eigenvectors. We used the loci separately for over-identification tests of the IV assumptions. Results: Each unit change in the polygenic risk score was associated with a -0.05 SD difference in memory score (95% CI: -0.058, -0.042). The conventional RD (-0.101, 95% CI: -0.119, -0.083) indicated large decreases in mortality per SD increase in memory. The IV estimate had the reverse sign but was imprecisely estimated (RD = 0.167; 95% CI: -0.107, 0.441). Conclusion: The IV and conventional estimates of the effect of memory on mortality had opposite signs, but we cannot rule out chance as an explanation for this contrast. With improved statistical power, genetic IVs may remediate the challenges in assessing the effects of memory deterioration on mortality.

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EDUCATIONAL DIFFERENCES IN LATE LIFE COGNITION TRAJECTORIES: ROLE OF SMOKING AND PHYSICAL ACTIVITY. *Elizabeth Grubert, Botoseneanu Anda, Benjamin Shaw (University at Albany (SUNY), Rensselaer NY 12144)

Cognitive impairment at older ages is reported as a primary cause of late life functional decline. Aging adults with low levels of education are at increased risk for cognitive impairment, but the reasons behind this increased risk are still unclear. The current study examines the impact of stability and change in two key health risk behaviors–smoking and physical inactivity–on educational differences in late life cognitive impairment trajectories. Data come from a nationally representative sample of adults born between 1931 and 1941 who were interviewed bi-annually between 1992 and 2008 for a total of 9 waves (N = 3424 respondents; 13696 observations). Hierarchical linear models with time-varying and time-constant covariates were used to define the trajectory of a global cognitive function score between 2002 and 2008. Physical activity trajectories, identified using group-based mixture modeling (persistent inactive, increasingly active, decreasingly active, and persistent active), and smoking patterns were assessed between 1992 and 2002. Our results show evidence of significant educational differences in cognitive ability that were stable over time. A history of persistent physical activity was associated with a modest slowing in cognitive decline over time, but smoking was not significantly associated with cognitive ability trajectories (intercept or slope). Together, these behaviors did not modify the observed association between education and later life cognitive ability. We conclude that although physical activity and smoking patterns are strongly associated with education, they are only weakly associated with cognitive impairment, and thus, are likely not responsible for the increased risk of cognitive impairment among individuals with low levels of education.

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USE OF EMERGENCY MEDICAL SERVICES ELECTRONIC RECORDS TO MONITOR HEALTH-RELATED EVENTS SUCH AS FALLS IN SKILLED NURSING FACILITIES IN NORTH CAROLINA. *Catherine Donovan, Frances Shofer, Antonio Fernandez, Larry Glickman (University of North Carolina, Chapel Hill NC 27599)

Objective: To evaluate the feasibility of using routinely collected emergency medical services (EMS) data to measure the frequency and pattern of health-related events (e.g. falls) in a state-wide population of persons residing in skilled nursing facilities (SNF), and as an indicator of health care quality or disease outbreaks. Introduction: Approximately 1.4 million adults 65 and older in the US, and over 35,000 individuals in NC, reside in SNFs. In NC, most nursing home residents are transported to other health facilities for routine or emergency care by EMS, and electronic records of each transport are updated daily and stored in a central data warehouse. Methods: Electronic records of all EMS transports in NC were obtained from the Prehospital Medical Information System for the period of January 2009 through December 2010. Records (N = 170,378) were selected if the incident address corresponded to the address of 354 NC SNFs, based on information obtained from the North Carolina Department of Health and Human Services. All EMS chief complaints indicating a fall were selected for further analysis. Results: 5,399 (4%) EMS transports were for falls, with the majority occurring among individuals in their eighties (median age = 84). Females were more likely to fall than males (Odds Ratio [OR] = 1.35, 95% Confidence Interval [CI]: 1.29-1.41) as were whites compared with blacks (OR = 3.07, 95% CI: 2.89-3.26). When falls were normalized to the number of beds per SNF, no association was found between Medicare quality rating and the number of EMS transports for falls. Conclusions: Routinely collected EMS records can be used to monitor patterns of health-related events among persons residing in SNFs. They may also be useful for identifying sudden unexpected increases in events related to criminal acts or infectious diseases as well as for assessing temporal trends related to health care quality in SNFs or changes in health care policy.

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CYTOMEGALOVIRUS INFECTION AND RISK OF AD IN OLDER AFRICAN AMERICANS AND CAUCASIANS. *Lisa Barnes, Ana Capuano, Allison Aiello, Arlener Turner, Robert Yolken, David Bennett (Rush University Medical Center, Chicago Il 60612)

Cytomegalovirus (CMV) is prevalent in older adults and has been implicated in many chronic diseases of aging. Its risk with incident Alzheimer's disease (AD) has not been reported. This study investigated the association of CMV serostatus with risk of AD and change in cognitive function in African Americans and Caucasians. Data come from three longitudinal cohort studies with identical study designs and data collection: the Rush Memory and Aging Project, Religious Orders study, and Minority Aging Research Study. A solid-phase enzyme-linked immunosorbent assay was used for detecting type-specific IgG antibody responses to CMV measured by optical density units from frozen serum. Participants had a mean age of 78.6 years (SD = 7.2) and a mean education level of 15.4 years (SD = 3.3). Of 849 participants, 73.4% had serologic evidence of CMV (89.0% African American, 68.2% Caucasian, $p < .001$). During an average of 5.0 years of follow-up, 93 persons developed AD. Scores based on normalized inverse probabilities were used in all models to reduce bias due to unbalanced distribution of confounders across race. CMV seropositivity was associated with a 2-fold increase in risk of AD (hazard ratio, 2.4; 95% confidence interval, 1.5-3.8), in models that controlled for age, sex, education, and race. In mixed effects models that controlled for the same covariates, CMV seropositivity was associated with a faster rate of decline in global cognition (estimate = -0.024, SE = 0.010, $p = .02$). These results suggest that CMV infection is associated with an increased risk of AD and a faster rate of cognitive decline in older populations. Because CMV prevalence is more common in African Americans, future studies should examine whether CMV may account for race differences in risk of AD. Future studies should also consider interventions targeting CMV, such as antivirals or development of vaccines, to assess whether intervening on CMV reduces risk of AD development and cognitive decline.

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INCREASED LATE-LIFE MORBIDITY INDEX AMONG OVERWEIGHT AND OBESE MEN MAY BE FULLY MEDIATED BY MIDLIFE LEVELS OF SERUM CHOLESTEROL COMPONENTS. *Uri Goldbourt, Moshe Hoshen, Ran Balicer, igal Hekselman, David Tanne (Tel Aviv University, Tel Aviv Israel)

The Charlson Comorbidity Index (CCI) was designed to develop a prospectively applicable method for classifying comorbid conditions which might alter the risk of mortality for use in longitudinal studies. Among a cohort of 10,059 men, apparently healthy tenured workers aged 40-65 in 1963, extensive biochemical, anthropometric,clinical and nutritional information was collected in 1963, 1965 and 1968. CCI was available for 75% of the surviving men in 2002, who were insured with the largest national HMO ("Clalit"). We grouped CCI into CCI score (CCIS) in 5 groups: CCI<3, =4, =5, =6 and CCI≥7 and examined the survivors' CCIS according to antecedent risk factor levels 37 years earlier. Among 2086 Clalit men surviving by 2002, using ordered logistic regression, "desirable" (20<BMI30) were associated with odds ratios (ORs) of 1.06, 1.22 and 1.31 of increased CCIS, respectively, relative to lean men (BMI<20) under proportional odds assumption, P for trend = 0.02. Adjusting for 1965 blood levels of HDL (OR = 0.88 per 1 SD increment, 95% CI 0.80-0.96) and non-HDL (OR = 1.15, 95% CI 1.04-1.26) cholesterol, the association of BMI in the year 1965 with 2002 CCIS was eliminated. Further adjustment for 1965 levels of SBP or DBP lowered the ORs associated with the non-lean BMI groups to 0.92, 0.94 and 1.00 (NS). Conclusion: Mid-life lipid components were related moderately to late-life comorbidity and eliminated a statistical association of the latter with increased mid-life weight.

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HEALTH-RELATED QUALITY OF LIFE IN OLDER ADULTS WITH DEPRESSION. *Jennifer Reneker, Vinay Cheruvu (Department of Epidemiology and Biostatistics, College of Public Health, Kent State University, Kent OH 44242)

Depression among older adults is often overlooked and if left untreated, can last for years. This can have serious consequences on Health-Related Quality of Life (HRQOL) and can increase the risk of morbidity and mortality. The objective of this research was to investigate the relationship between depression and HRQOL in aging individuals from a nationally representative sample. Cross-sectional data from the 2010 Behavioral Risk Factor Surveillance System (BRFSS) involving adults 65 years of age or older were used for this study (n = 35,668). The Patient Health Questionnaire 8 (PHQ-8) item scale was used to estimate the prevalence of current depression symptoms, classified as: "none," "mild," "moderate," and "severe." HRQOL constructs measuring "self-rated health," "physical health," & "social functioning" were the outcomes of interest. Logistic regression models were used to examine the association between current depressive symptoms and HRQOL outcomes, adjusting for all potential confounders. Data were analyzed in 2012 and accounted for complex sampling design of the BRFSS. Of the 35,688 older adults, 1.8% had severe, 3.0% had moderate, and 13.8% had mild depression. Current depression was significantly associated with poor HRQOL outcomes, after controlling for all potential confounders. Compared to individuals with no depressive symptoms, individuals with severe depressive symptoms were at a higher risk for poor HRQOL outcomes: [Odds Ratio (OR) for poor self-rated health: 14.6, 95% Confidence Interval (CI): 9.9 - 21.8]; [OR for poor physical health: 16.7, 95% CI: 11.8 - 23.5]; [OR for poor social functioning: 33.6, 95% CI: 23.8 - 47.5], followed by individuals with moderate, mild depressive symptoms (significant trend). Findings from this study provide valuable new insights into the relationship between current depressive symptoms and HRQOL and highlight the importance of public health interventions for aging individuals with depression.

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HIPPOCAMPAL CHANGES AND SUBSEQUENT DEPRESSIVE SYMPTOMS IN A COMMUNITY-BASED SAMPLE OF OLDER ADULTS. *Martine Elbejjani, Rebecca Fuhrer, Michal Abrahamowicz, Bernard Mazoyer, Fabrice Crivello, Christophe Tzourio, Carole Dufouil (McGill University, Department of Epidemiology, Biostatistics, and Occupational Health, Montreal QC Canada)

Several studies have reported a cross-sectional association between smaller hippocampal volume (HcV) and depression. However, the temporal sequence of the association is not understood. One proposed hypothesis is that hippocampal volume loss might act as a susceptibility factor for depression. This study aims to assess whether loss in HcV is associated with subsequent depressive symptoms in community-dwelling older adults. We used a prospective cohort of older adults (n = 1328, 65-80 years old) with two cerebral magnetic resonance imaging (MRI) scans taken four years apart (between t0 and t2). Linear mixed-models were used to estimate (i) the average association between yearly rate of HcV loss over four years and depressive symptoms (Center for Epidemiological Studies-Depression scale) measured biennially over the subsequent four years (at t2, t3, and t4) and (ii) the association between rate of HcV loss and rate of change in depressive symptoms. As such, the time of the 2nd MRI (t2) constitutes a temporal landmark between the loss in HcV, between the two MRI examinations, and depressive symptoms in the following four years. There was an average association between faster rate of HcV loss and subsequent higher depressive symptoms (coefficient = 0.54; 95% CI = 0.17, 0.90). In analyses of HcV loss and rate of change of depressive symptoms, we found that accelerated HcV loss was associated with higher concomitant (t2) depressive symptoms (coefficient = 0.45; 95% CI = 0.05, 0.86), but was not associated with the rate of change in depressive symptoms (coefficient = 0.04; 95% CI = -0.05, 0.21). Adjustment for potential confounders did not change these results. In additional analyses, we will control for selective loss to follow-up using inverse probability of censoring weighting. Faster HcV loss was associated with subsequent depressive symptoms overall and with concomitant (t2) depressive symptoms but did not predict symptoms worsening over time.

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TYPE 2 DIABETES, MORTALITY, AND COGNITIVE DECLINE AMONG OLDER MEXICAN AMERICANS. *Elizabeth Rose Mayeda, Mary Haan, John Neuhaus (University of California, San Francisco, San Francisco CA 94107)

Cognitive decline and diabetes are both associated with higher death rates. Prior studies of the association between diabetes and cognitive decline have not accounted for the dependence between cognitive decline and death. In this study, we examined the association between diabetes and cognitive decline in 1634 older Mexican Americans from the Sacramento Area Latino Study on Aging (age 60-101) followed for a mean of 6.4 years. Global cognitive function was assessed annually with the Modified Mini-Mental State Exam (3MSE). Because the distribution of 3MSE scores was left-skewed, we modeled the log transformation of errors on the 3MSE [log(3MSE errors)]. To account for the dependence between cognitive decline and death, we specified a joint model composed of two sub-models with shared parameters: a linear mixed effects model for cognitive decline and a piecewise exponential model for time to death. The annual rate of cognitive change followed a quadratic function, so a quadratic term for time was included in the linear mixed effects sub-model. Throughout the study, 48.2% of participants had diabetes and 22.8% died. Diabetes and rate of increase in log(3MSE errors) were both associated with higher death rates. In the joint model adjusted for socio-demographic characteristics and cardiovascular risk factors, diabetes was associated with more rapid annual increase in log (3MSE errors) (time: b = 0.039 log-errors; 95% confidence interval (CI): -0.003, 0.080; time squared: b = -0.004 log-errors; 95% CI: -0.009, 0.001). Results from a separate linear mixed effects model not accounting for death were similar (time: b = 0.038 log-errors; 95% CI: -0.004, 0.079; time squared b = -0.004 log-errors; 95% CI: -0.009, 0.001). Among older Mexican Americans, diabetes is associated with faster cognitive decline. Despite a strong association between cognitive decline and death, adjustment for death with joint models did not substantially affect risk estimates.

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OBJECTIVELY MEASURED LIFESPACE: THE LIFEMETER STUDY. *Amii Kress, Brian Schwartz, Thomas Glass (Johns Hopkins Bloomberg School of Public Health, Baltimore MD 21224)

Older adults are hypothesized to be more sensitive to local exposures and neighborhood contextual effects because they spend more time in their residential neighborhood. However, few empirical studies have tested this assumption. Most studies have relied on self-reported data, which is known to be subject to potentially severe bias. New methodology is needed to gather real-time, continuous, objective data on location and travel patterns to evaluate this hypothesis. We report on a new method based on continuous global positioning system (GPS) tracking of older subjects and propose a range of potentially useful metrics to study life-space. We quantified the proportion of time older adults spend in their residential neighborhood using data from the LIFEmeter Study, a cross-sectional study of 100 community-dwelling adults aged 60-80 years from 36 neighborhoods in Baltimore City, randomly selected from among participants in an ongoing longitudinal cohort study. Subjects wore GPS data loggers for 5 days. Usability and adherence to the devices was excellent; 89% of subjects had usable GPS data with a mean of 45 (SD = 14) hours of data and 14,428 (5,967) discrete data points per subject. Overall, among participants residing in Baltimore City (n = 77), 82% (Range 6-99%) of participants' waking time was spent within their residential neighborhood (defined by the Baltimore City Department of Planning in order to have spatial units that were recognizable by the community members). Four types of activity patterns were identified: activity in all directions around home; activity in one primary direction from home; reoccurring trips between home and one other location; and, minimal movement beyond one's residence. GPS devices are useful for quantitative and objective measurement of life-space in older adults. Improvements in life-space assessment will improve our ability to assess the enacted mobility functioning in older adults in addition to the role of neighborhoods in the aging process.

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BODY COMPOSITION IN RELATION TO HIP BONE LOSS AMONG RACIALLY/ETHNICALLY DIVERSE MIDDLE-AGED MEN. *Andre Araujo, Robert Chang, Shan Chen, Gerber Rachael, Nicholas Dagincourt, Elizabeth Suarez, Julia Akeroyd, Carrie Wager, Gretchen Chiu, Benedetta Bartali (New England Research Institutes, Inc., Watertown MA 02472)

Data on the influence of fat vs. lean tissue on fracture risk are mixed. Our Boston Area Community Health/Bone (BACH/Bone) Survey data show a strong cross-sectional association of lean mass (LM) vs. fat mass (FM) with bone strength in men, but longitudinal data are lacking. Data from the BACH/Bone Survey, a population-based cohort study of 1219 racially diverse men, were used to examine the relation of baseline total body LM and FM with decline in femoral neck bone mineral density (fnBMD) assessed by dual x-ray absorptiometry. Multivariable linear regression was used to examine the independent associations of baseline LM and FM (quartiles (Q) and continuous) with percent change in fnBMD, controlled for baseline fnBMD, age, race/ethnicity, income, smoking, type 2 diabetes mellitus, and self-rated health. 692 men (70% of eligible) with mean(SD) baseline age 51(12)y completed follow-up examinations 7.0(0.6)y later. Estimated(relative standard error; RSE) % decline in fnBMD was 5.0(0.2)% during follow-up (annualized, 0.71%/y), with steeper declines in men 70+y (6.8(0.9)%), and among black (6.0(1.1)%) and Hispanic (6.1(1.1)%) vs. white (4.8(1.1)%) men. Estimated(RSE) % declines in fnBMD were 4.4(0.5)% in LM Q1 vs. 5.2(0.5)% in Q4, whereas in FM Q1, fnBMD declined by 5.5(0.5)% vs. 4.7(0.5)% in FM Q4. In multivariable models, FM (Q, p = 0.05, continuous, p = 0.02) but not LM (Q, p = 0.12, continuous, p = 0.11) was significantly associated with change in fnBMD. Least-square means for FM quartiles were: Q1, -6.1%; Q2, -5.7%; Q3, -4.7%, and Q4, -4.2%. fnBMD declined 0.8(0.3)% for each 10kg decrease in FM. Similar yet insignificant results were observed for BMI. Associations did not vary by age or race/ethnicity. In conclusion, FM is an independent and strong predictor of decline in fnBMD, with elevated FM protective against bone loss in middle-aged men. Grant Support: R01AG020727.

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BODY COMPOSITION IN RELATION TO BONE MICROARCHITECTURE AMONG RACIALLY/ETHNICALLY DIVERSE MIDDLE-AGED AND OLDER MEN. *Elizabeth Suarez, Nicholas Dagincourt, Shan Chen, Gretchen Chiu, Rachael Gerber, Julia Akeroyd, Robert Chang, Carrie Wager, Mary Bouxsein, Andre Araujo (New England Research Institutes, Inc., Watertown MA 02472)

Recent studies suggest that obesity in men is associated with increased fracture risk, but few have examined the relation of body composition with bone microarchitecture. We obtained cross-sectional data from 692 men aged 38-86y enrolled in the Boston Area Community Health/Bone (BACH/Bone) Survey, a population-based cohort study of racially diverse men. Microarchitecture at the distal radius (N = 443) and tibia (N = 473) was measured by high-resolution peripheral quantitative computed tomography, with CVs <5%. Total body lean mass (LM) and fat mass (FM) were assessed by dual-energy x- ray absorptiometry. Multivariable linear regression was used to examine the independent associations of LM and FM with cortical and trabecular parameters, controlled for age, race/ethnicity, physical activity, self-rated health, smoking, and cancer. Mean(SD) age was 58.0 (11.6)y, BMI was 29.0(5.3)kg/m2, FM was 21.9(8.7)kg, and LM was 54.9 (8.1)kg. Bivariate and multivariable results were similar. In multivariable models, a 10kg increase in LM was associated with a significant increase of 0.07 and 0.22 in trabecular number (per 1/mm) in the distal radius and tibia, respectively. LM was significantly associated with higher trabecular density and total area, but lower cortical density and trabecular thickness in the distal tibia. FM was positively associated with trabecular number and negatively associated with cortical density and thickness in the distal tibia, but was not associated with any parameter in the radius. In conclusion, LM and FM appear to play strong, if complex, roles in determining bone microarchitectural properties in men. Overall, trabecular and cortical parameters in the weight-bearing tibia are more strongly related to body composition (especially LM) than those in the radius, consistent with the important role of mechanical loading in bone strength. Grant Support: R01AG020727

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CAUSAL PATHWAYS TO MORTALITY AMONG ELDERLY PATIENTS TREATED WITH ANTIPSYCHOTIC MEDICATIONS: A SYSTEMATIC REVIEW. *John Jackson, Schneeweiss Sebastian, Tyler J VanderWeele, Deborah Blacker (Harvard School of Public Health, Boston MA 02115)

Objective: To identify which of the following antipsychotic-induced major medical events contribute to mortality differences between first generation agents (FGAs) and second generation agents (SGAs) when used in older adults: stroke, ventricular arrhythmia, venous thromboembolism, myocardial infarction, pneumonia, and hip fracture; and to quantify their contribution. Design: Systematic Review. Data sources: Pubmed and Science Citation Index. Eligibility criteria: Randomized or observational studies of antipsychotic users; evaluated the risk of mortality or major medical events under study; was not restricted to schizophrenia or psychiatric inpatients; directly compared FGAs to SGAs or compared both to a non-user group; employed a "new user" design; was adjusted for confounders that were assessed prior to antipsychotic initiation; did not require survival after antipsychotic initiation for cohort entry. Results: Of the 1122 unique citations retrieved, we included 20 observational cohort studies, corresponding to 28 reported associations between antipsychotic type (FGA vs. SGA) and mortality or major medical events. Considering the rate of occurrence and case-fatality proportion for each major medical event, we identified hip fracture, stroke, myocardial infarction, and ventricular arrhythmias as potential intermediaries on the causal pathway from antipsychotic type to death. However, only one quarter of the mortality difference was explained by these major medical events. Conclusions: Hip fracture, stroke, myocardial infarction, and ventricular arrhythmias serve as plausible explanations for mortality differences between SGAs and FGAs. Future research should aim to better quantify the risk for these major medical events and their contribution to mortality.

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CHANGES IN DIABETES STATUS BETWEEN PREGNANCIES AND IMPACT ON NEWBORN OUTCOMES. *Nansi Boghossian, Edwina Yeung, Paul Albert, Pauline Mendola, S Katherine Laughon, Stephanie Hinkle, Cuilin Zhang (Changes in Diabetes Status Between Pregnancies and Impact on Newborn Outcomes, Rockville MD 20892)

Pregnancies complicated by gestational (GDM) or preexisting diabetes mellitus (DM) are at high risk for adverse newborn outcomes. The impact of GDM history, recurrence, or progression to DM on newborn risk is unknown. Medical record data on 62,013 repeat pregnancies were collected retrospectively from women who delivered at least 2 pregnancies in Utah (2002-2010). Poisson regression models with robust variance estimators were used to estimate relative risks (RR) of large for gestational age (LGA), preterm birth (<37 wks) and respiratory distress syndrome (RDS) adjusting for study site, maternal age, race, parity, prepregnancy BMI and smoking status. Compared to women with no previous GDM, GDM in the previous pregnancy but not in the current one increased the risk of LGA [RR = 1.2, 95% confidence interval (CI) = 1.1, 1.4] and preterm birth (RR = 1.2; 95% CI = 1.0, 1.5). Risk estimates were higher for recurrent GDM [LGA (RR = 1.7; 95% CI: 1.5, 1.9); preterm birth (RR = 1.7; 95% CI: 1.4, 2.0)] than pregnancies with current GDM only [LGA (RR = 1.4; 95% CI: 1.3, 1.6); preterm birth: (RR = 1.4; 95% CI: 1.2, 1.6)]. Women with a previous GDM that progressed to DM in the current pregnancy had increased risks of LGA (RR = 2.0, 95% CI: 1.7, 2.4), preterm birth (RR = 1.8, 95% CI: 1.4, 2.3), and RDS (1.7, 95% CI: 1.1, 2.6) compared to women with no previous GDM and no current DM. GDM in a previous pregnancy alone without recurrence may still confer an increased risk for LGA and preterm birth. Pregnancies complicated by GDM that progress to DM have the highest risks of adverse newborn outcomes.

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EFFECTS OF TAIWAN STYLE FRUCTOSE-RICH BEVERAGES CONSUMPTION ON INSULIN RESISTANCE IN ADOLESCENTS. *Wei-Ting Lin, Meng-Hsueh Chen, Chun-Ying Lee, Hsiao-Ling Huang, Tsung-Yun Liu, Chien-Hung Lee (National Yang-Ming University, Taipei Taiwan (ROC))

Hand-shaken beverage shops (derived from bubble tea sales) are densely in position in areas within a short walking distance from the residences and schools, exposing adolescents to immediate surroundings with high and easy Taiwan style fructose-rich beverages (FRB) accessibility. Insulin resistance (IR) has an imperative role in the diabetogenic process. Studies showed that people with IR in youth are at increased risks of developing type 2 diabetes in adult life. To investigate the effect of FRB intake on IR among adolescents in Taiwan, we evaluated data from 1454 representative adolescents who were multistage-sampled from 36 junior high schools. Detail demographic, physical and dietary variables, and anthropometric and clinical outcomes were collected. Data was analyzed using multivariate regression and logistic models adjusted for the complex survey design and covariates. An increased level of sugar-sweetened beverage intake was associated with an increased level of body mass index, body adiposity index, serum uric acid (SUA), original homeostasis model assessment of insulin resistance (HOMA1-IR), updated HOMA nonlinear computer model (HOMA2-IR), HOMA2 of percentage beta cell function and HOMA2 of insulin sensitivity. As compared to non-drinkers, heavy FRB drinkers had a 0.45 and 0.26 higher level of HOMA1-IR and HOMA2-IR, respectively. The effects of FRB on HOMA1-IR and HOMA2-IR were also found to be strengthened among adolescents with obesity or with hyperuricemia (1.15-2.33 increases in HOMA1-IR and 0.62-1.26 increases in HOMA2-IR, respectively). While type 2 diabetes does not become clinically apparent until the adulthood, our data stress the effect of high FRB intake on IR in adolescents, particularly in those with obesity or hyperuricemia.

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ADOLESCENT TESTOSTERONE, MUSCLE MASS AND GLUCOSE METABOLISM: EVIDENCE FROM "CHILDREN OF 1997" IN HONG KONG. *Wei Wei Hou, Tai Hing Lam, Gabriel M Leung, Catherine Mary Schooling (Department of Community Medicine, University of Hong Kong, Hong Kong SAR China)

Diabetes rates are high in Asia despite relatively low rates of obesity. Muscle mass plays an important role in glucose metabolism and also tends to be lower in Asians. Peak muscle mass is attained in adolescence and influenced by sex-steroids. This study tested the hypothesis that pubertal testosterone is negatively associated with glucose and insulin resistance, with the association mediated by muscle mass. Participants aged 15 (278 males and 223 females) were recruited from the Chinese "Children of 1997" birth cohort in Hong Kong. Multivariable linear regression was used to examine the adjusted cross-sectional association of testosterone with fasting glucose, fasting insulin and homeostasis model assessment - insulin resistance (HOMA-IR). The Sobel-Goodman test was used to assess any mediation by muscle mass (obtained from a dual-energy X-ray absorptiometry scan). Total testosterone (nmol/L) was negatively associated with insulin (-0.35 mIU/L, 95% confidence interval (CI) -0.46 to -0.24) and HOMA-IR (-0.070, 95% CI -0.093 to -0.047), but not with glucose (-0.006 mmol/L, 95% CI -0.012 to 0.0002), adjusted for sex. Total testosterone was positively associated with skeletal muscle index (SMI) (0.27%, 95% CI 0.21 to 0.34). SMI was negatively associated with insulin (-0.73 mIU/L, 95% CI -0.86 to -0.60), HOMA-IR (-0.15, 95% CI -0.17 to -0.12) and glucose (-0.013 mmol/L, 95% CI -0.020 to -0.005). SMI mediated about 50% of the association of testosterone with insulin and HOMA-IR. The associations were little changed by additional adjustment for birth weight, parental education and mother's migrant status, or by the use of calculated free or bioavailable testosterone instead of total testosterone. Adolescent glucose metabolism is influenced by testosterone partially via skeletal muscle mass. Adolescence may be a sensitive period for the development of diabetes, where interventions to increase muscle mass could have long-term protective effects.

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EFFECTS OF FRUCTOSE SWEETENED BEVERAGES INTAKE ON RETINOL BINDING PROTEIN 4 AMONG ADOLESCENTS. *Meng-Hsueh Chen, Te-Fu Chan, Wei-Ting Lin, Yi-Ling Chen, Chun-Ying Lee, Hsiao-Ling Huang, Chien-Hung Lee (Kaohsiung Medical University, Kaohsiung Taiwan)

The density of chain convenience stores in Taiwan is among the highest in the world. On average, there is one convenience store for every 2,300 people in the respective community. This forms an environment that is accessible to sugar sweetened beverages (SSB) for adolescents. Retinol binding protein 4 (RBP4) is secreted largely by mature adipocytes, and was found to be up-regulated in adipose tissue. Previous studies have shown that RBP4 is a potential mediator of obesity-induced insulin resistance and metabolic risk. To investigate the effect of SSB intake on RBP4 in adolescent, a total of 200 subjects, aged 12-15 years, were randomly selected from the existing large-scale study conducted to monitor Multilevel Risk Profiles for Adolescent Metabolic Syndrome in Taiwan. Serum RBP4 was measured by an ELISA approach. Detail demographic, physical and dietary variables, and anthropometric and clinical outcomes of each adolescent were collected. Data was analyzed using multivariate regression and logistic models adjusted for covariates. An increased level of SSB consumption was found to be associated with an increased level of body mass index (BMI), serum uric acid (SUA) and RBP4. As compared to non-drinkers, adolescents who consumed fructose-rich beverages (11.0 to 12.1 ng/ml increases) and sucrose-fructose mixed beverages (12.1 ng/ml increase) respectively had a significantly higher level of RBP4, even the influences of BMI and SUA were adjusted for. We also found about 6.7% of the effect of fructose-rich beverages on RBP4 was accounted for by SUA. Our data suggests that fructose-containing beverage intake has a substantial effect on RBP4, through which SSB might influence insulin resistance and metabolic risk in adolescents.

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CANCER INCIDENCE IN COHORT OF 36379 TYPE 2 DIABETICS IN MINHANG DISTRICT. S Hong Fang, *Huilin Xu, Yujie Yan, Liyun Zhao, Yinan Liu, Jie Zhou, Yanping Zhao, Na Wang (Minhang District Center for Disease Control and Prevention, Shanghai China)

Although the association between diabetes and cancer has been proposed for decades, little is known about cancer incidence among diabetics in China. The authors investigated the cancer incidence in 36379 type 2 diabetics derived from the program of enrolment and standardized management based on local electronic information system during 2004 to 2010, in Minhang District, Shanghai. The new case of cancer was ascertained by the Shanghai Cancer Registry. U test and standardized incidence ratios (SIR) was used to compare the cancers incidence for diabetics and general residents. The cohort consisted of 16166 men and 20213 women with an average age of about 58.4 years and 59.4 years for men and women respectively. During a mean follow-up of 3.7 years, 1205 cancer cases were observed. The crude cancer incidence rate was 955.21per 100000 py in men and 829.57 per 100000 py in women. The SIR revealed that the cancer incidence was higher in this cohort of diabetics than in the general population, which was 1.98(95% confidence interval [1.82-2.14]) in men and 1.94(95% confidence interval [1.19-2.09]) in women. The SIR of cancers was specifically higher for diabetics with lower Diagnosis age. For diabetics diagnosed at their 20s and 30s, the accordingly SIR was 28.30(95% confidence interval [10.38-62.00]) and 5.47(95% confidence interval [3.57-8.01]), respectively. Among prevalent cancer, the standardized incidence of prostate, colon, kidney cancer in men and breast, stomach, corpus uteri cancer in women in diabetics was significantly higher than those of general residents. This study suggested a sharply increased risk for specific cancer and certain age group in diabetics, potential mechanisms for which need further studies.

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RISK OF BIRTH DEFECTS ASSOCIATED WITH MATERNAL PREGESTATIONAL DIABETES: A POPULATION-BASED COHORT STUDY IN NORTHERN ITALY. *Marco Vinceti, Carlotta Malagoli, Rossella Rodolfi, Kenneth Rothman, Aurora Puccini, Mark Lunt, Gianni Astolfi, Elisa Calzolari, Fausto Nicolini (CREAGEN - University of Modena and Reggio Emilia, Reggio Emilia Italy)

Maternal diabetes preceding pregnancy, whether type-1 or type-2, appears to increase the risk of birth defects in the offspring, though several aspects of this relation are still unknown or controversial. We conducted a large population-based cohort study in the Northern Italy region of Emilia-Romagna using administrative databases and a Birth Defects Registry. From hospital discharge records we identified all diabetic pregnancies during 1997-2010, and a population of non-diabetic parturients matched for age, province of residence, year and hospital of delivery. We collected where available information on drug prescriptions, from which we inferred the type of diabetes. We found 62 malformed infants out of 2,269 births among diabetic women, and 162 out of 10,648 births among non-diabetic women. The prevalence ratio (PR) of malformation associated with maternal pregestational diabetes was 1.73 (95% confidence interval 1.28-2.33). Period of birth and type of diabetes strongly influenced the PR, with higher values estimates in the earliest periods and in type-2 diabetic women compared with type-1 diabetic mothers. The latter group exhibited no excess risk in the most recent period, 2006-2010, possibly owing to improvements in metabolic control over time. Most subgroups of anomalies had PRs above 1, but relevant and statistically more precise excess risks were seen for cardiovascular, genitourinary, musculoskeletal, and chromosomal abnormalities. The present study indicates that maternal diabetes increases the risk of specific birth defects in offspring, particularly for type-2 diabetes, whereas for type-1 diabetic mothers in the most recent years, this was not the case.

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DOES THE FEMALE FETUS AFFECT INSULIN RESISTANCE IN THE MOTHER? *Lin Xiao, Jin-Ping Zhao, Anne Monique Nuyt, William D Fraser, Zhong-Cheng Luo (CHU Sainte-Justine, University of Montreal, Montreal QC Canada)

Substantial evidence indicates that girls are more insulin resistant than boys in utero, but whether the female fetus may affect insulin resistance in the mother is unknown. In a prospective singleton pregnancy cohort ($n = 299$), we explored maternal insulin resistance by fetal sex, based on maternal plasma glucose and insulin concentrations in the 50 g oral glucose tolerance test (OGTT) blood at 24-28 weeks gestation. Comparing women bearing a female vs. male fetus, maternal OGTT blood insulin concentrations were significantly higher (mean ± SD: 71.7 ± 64.8 versus 51.0 ± 46.1 mU/L, $p = 0.02$), despite similar glucose levels (mean ± SD: 116.4 ± 27.2 versus 117.0 ± 32.0 mg/dL). Glucose-to-insulin ratio was significantly lower in women bearing a female fetus (2.6 ± 2.0 versus 4.6 ± 9.3 mg/dL/mU/L, $p = 0.003$). The differences by fetal sex in maternal plasma insulin concentration ($p = 0.001$) and glucose-to-insulin ratio ($p = 0.001$) remained significant after adjusting for maternal characteristics (body mass index, age, ethnicity, education, parity, smoking and alcohol use). The preliminary data indicate that the female fetus may increase maternal insulin resistance, consistent with some previous reports of greater secretion of certain placenta-derived insulin antagonist hormones in women bearing a female versus male fetus.

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THE ASSOCIATION BETWEEN PSYCHOLOGICAL PROBLEMS AND THE RISK OF DIABETES IN CHILDREN AGED 9. *Su Hyun Park, Hye Ah Lee, Eui Jung Kim, Eun Ae Park, Su Jin Cho, Hae Soon Kim, Hye sook Park (Ewha Womans University, Seoul Republic of Korea)

Objectives: Type 2 diabetes (T2D), or non-insulin-dependent diabetes, is the most common type of diabetes, typically occurring at a later age, although it can occur at any age. According to the World Health Organization (WHO), the prevalence of T2D among children is gradually increasing worldwide, making it one of the most prominent issues in medicine today. Psychological problems are known result from poor diabetes control. Conversely, recent evidence has suggested that psychological problems may increase the risk of diabetes. The purpose of this study was to identify the relationship between the risk of diabetes and psychological problems, especially for nine-year-old children that show symptoms of anxiety and depression byconducting the cross-sectional study. Methods: The data was collected from the Ewha Birth & Growth Cohort Study. A total number of 141 children aged 9 were asked to a answer several self-report questionnaires. These included the Spielberger State-Trait Anxiety Inventory (STAI), used to measure anxiety symptoms; and the Children's Depression Inventory (CDI) used to assess self-rated symptoms of childhood depression. As an outcome, the homeostasis model assessment of insulin resistance index (HOMA-IR) was calculated to estimate insulin resistance. Analysis of variance (ANOVA) was performed, using STATA statistical software. Results: The relationship between psychological disorders such as anxiety or depression and the risk of diabetes in children appeared to have a slightly U-shaped relationship after adjusting for potential confounders (e.g. age, race, sex, income, BMI, education). The mean values of HOMA-IR in the first tertile of STAI and CDI; 1.95 & 2.02 were higher than the mean value of HOMA-IR in the second of STAI and CDI; 1.83. Conclusions: In this study, results showed that anxiety and depression symptoms may increase the risk of developing diabetes. The limitation of this study was that the sample population was small. Further studies need to be conducted with a larger sample size. Acknowledgement: This work was supported by National Research Foundation of Korea Grant funded by the Korean Government (2010-0026225)

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AGE AT MENARCHE, LEG LENGTH, AND TYPE 2 DIABETES IN BRAZILIAN ADULTS: FINDINGS FROM THE BRAZILIAN LONGITUDINAL STUDY OF ADULT HEALTH (ELSA-BRASIL). *Noel Mueller, Bruce Duncan, Estela Aquino, Dora Chor, Sandhi Barreto, Maria Inês Schmidt (Universidade Federal do Rio Grande do Sul, Post Graduate Program in Epidemiology, Porto Alegre RS Brasil)

Studies in Caucasian and Asian populations have suggested earlier puberty is associated with a higher risk of type 2 diabetes (T2D). There have been no studies on this topic from Latin America, where ongoing nutritional transitions may have unique influence on developmental factors and diabetes. In this study we examined leg length (LL) and age at menarche (AAM), as markers of development and pubertal timing, in relation to T2D. We used information from ELSA-Brasil, a cohort of 15,105 Brazilian adults, aged 35-74y at baseline exam (2008-2010). Logistic regression was used to compute odds ratios (OR) and 95% confidence intervals for diabetes according to AAM (<11y, ≥11y) and LL (quintiles) after adjusting for baseline age, study center, race/color, maternal education, participant education, income, parity, menopausal status/age, physical activity, smoking status, sitting height, and LL or AAM (model dependent). In a potential mediation model, we further adjusted for BMI and gluteal and waist circumferences. Women with earlier menarche had 50% (21-86%) higher odds of diabetes than those with later menarche; this being attenuated to 25% (0-57%) after adjustment for concurrent adiposity measures. We also observed an inverse linear association between LL and diabetes, adjusted for AAM, prior to ($p = 0.01$) and after ($p = 0.03$) additional adjustment for adiposity measures. Compared to those in the 1st LL quintile, women in the 5th quintile presented diabetes less frequently after full adjustment (OR = 0.67; 0.53-0.85; p for trend < 0.01). Associations of similar magnitude were observed for men (p for trend < 0.01). Thus, leg length and age at menarche are independently associated with T2D, suggesting these developmental markers reflect distinct early-origin pathways to diabetes. Further research is needed to determine the causal factors driving variation in childhood growth and maturation, as these may provide opportunities for primordial prevention of diabetes.

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VERY LOW AND LOW BIRTH WEIGHT ARE ASSOCIATED WITH HIGHER RISK OF TYPE 2 DIABETES IN U.S. BLACK WOMEN. *Edward Ruiz-Narvaez, Julie R Palmer, Lauren A Wise, Hanna Gerlovin, Varsha G Vimalananda, James L Rosenzweig, Lynn Rosenberg (Slone Epidemiology Center at Boston University, Boston MA 02215)

Previous studies have reported an increased risk of type 2 diabetes (T2D) among individuals with low birth weight. However, there are no prospective studies of this relation in U.S. black women, a population that is disproportionately affected by T2D. We assessed the association of birth weight with incident T2D in the Black Women's Health Study, an ongoing prospective cohort study that began in 1995 (baseline). We used Cox proportional hazard models to estimate incidence rate ratios and 95% confidence intervals (CI) for T2D across categories of birth weight (very low (≤1500 g), low (1500-2499 g), normal (2500-3999 g; referent), high (4000+ g)). Models were adjusted for age, time period, parental education, maternal age at birth, and energy intake. The present analysis included 21,958 women without a diagnosis of T2D at baseline and who reported their birth weight on a self-administered questionnaire in 1997; 2.4% had very low birth weight, 23.8% had low birth weight, 65.9% had normal birth weight, and 7.8% had high birth weight. A validation study using birth registry data indicated that self-reported birth weight was accurate. During 16 years of follow-up (1995-2011), there were 2,368 incident T2D cases. Women with very low birth weight had a 61% higher risk of T2D (95% CI = 1.24, 2.09) relative to women with normal birth weight; and women with low birth weight had a 24% higher risk of T2D (95% CI = 1.12, 1.37). No association was observed for high birth weight. Further adjustment for body mass index (kg/m^2) did not appreciably affect the estimates. In summary, women with very low or low birth weight had a higher risk of T2D, and the association did not appear to be mediated through adult body mass index.

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EVALUATION OF PHARMACOLOGICAL MANAGEMENT FOR TYPE-2 DIABETES POST-MYOCARDIAL INFARCTION. *Daniela Moga, Emily Brouwer, Ekim Ekinci, Xiang Zhang (Department of Pharmacy Practice and Science, College of Pharmacy and Department of Epidemiology, College of Public Health, University of Kentucky, Lexington KY 40536)

OBJECTIVES: Previous research suggests elderly patients with type 2diabetes mellitus (T2DM) are likely discharged without anti-diabetic medication (ADM) after an admission for myocardial infarction (MI). Our study aimed to evaluate ADM use post-MI in a commercially insured population. Methods: We assembled a nation-wide population-based cohort of patients with T2DM continuously enrolled by a private insurer between January 2007 and December 2009. T2DM was defined based on diagnosis codes and pharmacy claims for an ADM. We identified patients who experienced MI (ICD-9 code 410.xx) during our study period and evaluated ADM treatment before and after the cardiac event. We described medication utilization and investigated changes in medication use from pre- to post-MI. Logistic regression and resulting odds ratios (OR) with associated 95% confidence intervals (CI) were used to evaluate factors predicting treatment post-MI. Results: We identified 25,136 diabetic patients that experienced MI. Prior to MI, over 30% of the patients had a prescription for ADM, with approximately 12% receiving multiple drug regimens. The majority of the patients were treated with metformin (42%), followed by a sulfonylurea agent. Post-MI, 34% were treated; of the 75% with a prescription within 30 days, 35% received metformin. The median time from discharge until the first prescription fill was 25 days (interquartile range = 62). About 29% of those treated pre-MI, did not receive medication post-MI; about 1 in 8 patients initiated ADM within 30 days post-MI. Demographic characteristics and pre-MI treatment predicted treatment after MI. Older patients were less likely to fill a prescription post-MI (adjusted OR = 0.974; 95% CI: 0.972-0.977). Conclusion: Many T2DM patients experiencing MI are not discharged on previously prescribed ADM. Assessment of short and long-term outcomes in patients not receiving ADM post-MI, particularly in the elderly, warrants further investigation.

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ASSOCIATION BETWEEN SERUM 25-HYDROXYVITAMIN D LEVEL AND INSULIN RESISTANCE IN AN ELDERLY KOREAN POPULATION. *Bo Mi Song, Hyeon Chang Kim, Yumie Rhee, Yoosik Youm, Chang Oh Kim (Department of Public Health, Yonsei University College of Medicine, Seoul Korea)

Introduction: A low serum vitamin D concentration has been reported to be associated with increased risk of diabetes mellitus. But the relationship with 25-hydroxyvitamin D [25(OH)D] level and insulin resistance has not been ascertained in the Korean elderly population. The purpose of this study was to investigate the association between 25(OH)D level and insulin resistance in community-living elderly Koreans. Methods: This study used data from the Korean Urban Rural Elderly (KURE) study. In 2011 study, 927 participants aged 65 years or older completed baseline health examinations. Participants were recruited from an urban and a rural communities. After excluding two individuals missing 25(OH)D value, cross-sectional analyses were conducted for 925 participants (302 men and 623 women). Plasma glucose and serum insulin levels were measured from overnight fasting blood samples and homeostasis model assessment for insulin resistance (HOMA-IR) was calculated using them. Fasting glucose, insulin and HOMA-IR were log-transformed for parametric tests. Results: In men, serum 25(OH)D level was significantly associated with HOMA-IR ($\beta = -0.01$, $p = 0.027$) even after adjustment for age, body mass index, smoking status, alcohol intake and regular exercise. However, there were significant differences in serum 25(OH)D level (18.68 vs. 26.39 ng/ml; $p < 0.001$) and HOMA-IR (1.58 vs. 1.04; $p < 0.001$) between urban and rural areas. After additional adjusting for residential area, the association was not significant ($\beta = -0.001$, $p = 0.767$). In women, the association between 25(OH)D and HOMA-IR was not significant before ($p = 0.238$) and after ($p = 0.929$) adjustment for residential area. Conclusion: Our findings suggest that serum 25(OH)D level is not independently associated with insulin resistance in elderly Koreans.

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PERINATAL OXIDATIVE STRESS AFFECTS FETAL GHRELIN LEVELS. *Zhong-Cheng Luo, Jean-Francois Bilodeau, Anne-Monique Nuyt, William Fraser, Francois Audibert, Jin-Ping Zhao, Lin Xiao, Pierre Julien, Emile Levy (Sainte-Justine Hospital Research Center, University of Montreal, Montreal QC Canada)

The prenatal period is considered a critical developmental window in "programming" the vulnerability to obesity and "metabolic syndrome"related disorders. The mechanisms remain unclear. Perinatal oxidative stress may affect the expression of certain redox-sensitive gene products and "program" such susceptibility. This study investigated (for the first time) whether perinatal oxidative stress may affect fetal circulating levels of ghrelin - an important hormone regulating appetite and energy balance . Indices of oxidative stress (F2-isoprostanes, malondialdehyde (MDA)) were measured in maternal (24-28 weeks gestation) and cord blood in 255 singleton pregnancies. Plasma ghrelin concentrations were significantly higher in cord versus maternal blood (median: 392 versus 132 pg/ml), and were strongly correlated ($r = 0.50$, $p < 0.0001$). Indices of oxidative stress were highly correlated in maternal versus fetal cord blood ($r = 0.35$ for MDA, $r = 0.57$ for F2-isoprostanes, all $p < 0.0001$). Adjusting for gestational age at blood sampling and cord blood glucose concentration, consistent negative correlations were observed in cord plasma ghrelin levels with indices of oxidative stress in both maternal blood ($r = -0.37$, $p < 0.0001$ for MDA; $r = -0.17$, $p = 0.01$ for F2-isoprostanes) and cord blood ($r = -0.15$, $p = 0.02$ for MDA; $r = -0.28$, $p < 0.0001$ for F2-isoprostanes). Most observed associations remain significant after adjusting for maternal and pregnancy characteristics. The data consistently suggest that perinatal oxidative stress may suppress ghrelin expression during fetal life in humans, which may be a mechanistic link in programming the susceptibility to obesity and metabolic syndrome related disorders.

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ALL-CAUSE, CARDIOVASCULAR, AND CANCER MORTALITY IN POSTMENOPAUSAL WHITE, BLACK, HISPANIC, AND ASIAN WOMEN WITH AND WITHOUT DIABETES IN THE U.S.: THE WOMEN'S HEALTH INITIATIVE 1993-2009. *Yunsheng Ma, James Hébert, Jo Ann Manson (University of Massachusetts Medical School, Worcester MA 01545)

Objective: Using data from the Women's Health Initiative (WHI), we compared all-cause, cardiovascular (CVD), and cancer mortality in White, Black, Hispanic, and Asian postmenopausal women with and without diabetes. Research Design and Methods: Race/ethnicity, diabetes status, total and specific mortalities were obtained from 158,833 postmenopausal women recruited from 1993-1998 and followed up until August 2009. Comparisons of all-cause, CVD, and cancer mortality by self-reported diabetes status and by race/ethnicity were made using Cox proportional hazard models from which hazard ratios (HRs) and 95% confidence intervals (CI) were computed. Results: With an average age of 63 at baseline, WHI participants included 84.1% White, 9.2% Black, 4.1% Hispanic, and 2.6% Asian. The percentages of women with prevalent or incident diabetes from study enrollment to August 2009 were, in decreasing frequency: 27.1% for Blacks, 20.8% for Hispanics, 15.9% for Asians and 11.7% for Whites. Within each racial/ethnic subgroup, women with diabetes had approximately 2 to 3 times higher risk of all-cause, CVD and cancer mortality as compared to those without diabetes. However, the HRs for mortality outcomes were not significantly different between race/ethnic subgroups according to diabetes status. Population attributable risk percentages (PARP), which take into account both the prevalence of diabetes and HRs associated with the disease, indicated that for all-cause mortality, Whites had the lowest PARP [11.1 (95% CI: 10.1-12.1)] versus Blacks [19.4 (15.0-23.7)] and Hispanics [23.2 (14.8-31.2)], while the PARP was 12.9 (4.7 – 20.9) for Asians. Conclusions: Postmenopausal women with diabetes had a higher risk of all-cause, CVD, and cancer mortality when compared with postmenopausal women without diabetes. Both Black and Hispanic women are at higher-than-average risk of developing diabetes and have higher proportions of all-cause mortality attributable to diabetes compared to Whites. Because of "amplifying" effect of diabetes prevalence, efforts should focus on prevention of type 2 diabetes.

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THE MICROCLINIC HEALTH PROGRAM: A SOCIAL NETWORK-BASED INTERVENTION FOR WEIGHT LOSS AND DIABETES RISK MANAGEMENT. *Marta Prescott, Daniel Zoughbie, Katie Watson, Nancy Bui, Rami Farraj, Nadia Elkarra (Mailman School of Public Health, Columbia University, New York NY 10032)

Obesity and behavioral risk factors have been shown to aggregate and propagate via social networks. We aimed to examine the ability of a program, the Microclinic Health Program, to harness organic social structures by determining the extent to which change in clinical markers that occurred during the program was clustered within social layers. The program was conducted among 720 individuals who participated in the 4-month type-2 diabetes education program in Amman, Jordan. All subjects participated with 2-8 friends or family members (a microclinic) and had diabetes, were at-risk for diabetes, or had a loved one with diabetes. Clinical markers (weight, Body Mass Index [BMI], and Hemoglobin A1c [HbA1c]) were measured at baseline and at the end of the program. We used multivariable multi-level linear regression to examine the change in clinical markers as well as examine the clustering of change within social layers (microclinics, classes, or cohorts). At the end of the program, results indicated decreased weight (Beta [B]:-1.38 kg; 95% confidence interval [CI]: -1.73, -1.04), BMI (B:-0.55 kg/m2; 95% CI -0.69, -0.41), and HbA1c (B:-0.48%; 95% CI -0.61, -0.34). Additionally, the trajectories of change in these risk factors were clustered in the social layer within microclinic groups (Intraclass correlation [ICC] = 57.7% weight loss, ICC = 52.5% for BMI decrease, and ICC = 35.3% for HbA1c). Based on the clustering of change, our results suggest that the program successfully harness an organic social-network to promote improvements in diabetes management. Such a social network-based intervention may be a promising tool to propagate healthy behaviors for diabetes and obesity prevention throughout a community.

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SELF-RATED HEALTH AND ALL-CAUSE MORTALITY AMONG MIDDLE AGED AND OLDER ADULTS WITH AND WITHOUT DIABETES, NATIONAL HEALTH INTERVIEW SURVEY, 1997-2006.

*Keri Norris, Gloria Beckles, Yiling Cheng, Sharon Saydah, Giussepina Imperatore (Centers for Disease Control and Prevention, Atlanta GA 30341)

Self-rated health (SRH) is predictive of increased mortality risk. Adults with diabetes (DM) are more likely than those without to report fair/poor health and have higher mortality. Few studies have compared the SHR-mortality relationship among adults with/without DM. We examined the relationship between SRH and mortality in persons with and without DM. We investigated whether demographic, behavioral, clinical or healthcare access factors mediated the association. The study included adults aged 40 years and older with DM (n = 11781) and without DM (n = 108,179) who participated in the nationally-representative National Health Interview Surveys (1997-2003) and mortality follow-up through December 31, 2006. SRH was measured using the single-item self-assessment of health. SRH responses were dichotomized as low (fair/poor) and high (excellent, very good, good). We used Cox proportional hazards regression to estimate hazard ratios (HR) for all-cause mortality by DM status, controlling for age, sex, race/ethnicity, socio-economic and marital status, health insurance coverage, binge drinking, smoking status, body mass index, functional limitations, and history of cardiovascular diseases or cancer. In addition, for people with DM, models also included DM treatment mode and time since diagnosis. The unadjusted mortality HR for participants with low SRH compared to those with high SRH was 2.21 (95% confidence interval [CI] 2.00-2.44) in people with DM and 3.92 (95% CI 3.72-4.13) among those without DM. Adjusted HRs were attenuated but remained statistically significant for people with DM (1.52, 95% CI, 1.30-1.78; $p < 0.05$) and without DM (1.87, 95% CI, 1.71-2.05; $p < 0.05$). Low SRH predicts increased risk of death, regardless of DM status. Assessment of SRH may identify individuals needing intensified health promotion efforts.

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PERCEPTIONS OF DIABETES MANAGEMENT: DO PATIENTS AND PHYSICIANS AGREE?

*Roberta Figueiredo, Frank Snoek, Sandhi Barreto (Universidade Federal de Minas Gerais, Belo Horizonte, Brazil)

Physician-patient relationship is a crucial element of effective chronic illness care. However, effective communication is complex because professional's and patient's perspectives may differ. This study aimed to explore to what extent patients with diabetes agree with their physicians on diabetes management and whether the agreement varies according to patients' sociodemographic characteristics. A cross-sectional study was conducted among patients with diabetes and their Family Health physicians in 108 healthcare centres in Belo Horizonte, Brazil. Patients and physicians were interviewed face-to-face using standard questionnaires. Physicians were unaware of which of their patients would be interviewed. Their responses were compared using descriptive statistics and Cohen's weighted kappa. 282 patient-physician pairs were included. Kappa coefficients were often low, the highest was found for presence of diabetic foot and the lowest for kidney disease. Physicians tended to overestimate patients' risk of diabetes complications and underestimate patients' adherence to all diabetes self-management activities as well as diabetes control. Moreover, the agreement rate regarding adherence to diet, foot care and medicine prescriptions was significantly higher among male, younger and higher educated patients. Results indicate that physicians' recommendations are generally poorly apprehended by their patients, especially by the lower educated, compromising the goal of patient-centred care. Educational programmes need to incorporate strategies to improve the comprehension and effectiveness of physician-patient communication, especially with the most socially vulnerable groups.

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GENDER AND RACIAL/ETHNIC DIFFERENCES IN THE ASSOCIATIONS OF URINARY PHTHALATE METABOLITES WITH DIABETES BIOMARKERS: NHANES 2001-2008.

*Tianyi Huang, Aditi Saxena, Tamarra James-Todd (Division of Women's Health, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston MA 02120)

Women and minorities are more likely to be exposed to higher levels of phthalates, endocrine disrupting chemicals that may be associated with diabetes. To explore the role of phthalates in progression to diabetes and their contributions to gender and racial disparities in diabetes prevalence, we analyzed CDC data from 3083 non-diabetic, non-pregnant participants ages 12-80 in the National Health and Nutrition Examination Survey (NHANES) 2001-2008. We used median regressions to assess the associations between 6 urinary phthalate metabolites [mono-ethyl phthalate (MEP), mono-benzyl phthalate (MBzP), mono-n-butyl phthalate (MnBP), Mono-isobutyl phthalate (MiBP), mono-(3-carboxypropyl) phthalate (MCPP) and di-2-ethylhexyl phthalate (DEHP)] and 3 diabetes biomarkers including fasting blood glucose (FBG), fasting insulin and Homeostatic Model Assessment (HOMA-IR), controlling for urinary creatinine as well as a number of sociodemographic and dietary factors. Stratified analyses were conducted to compare the gender- and race-specific estimates for the associations. MnBP, MiBP, MCPP and ΣDEHP showed significant positive associations with FBG, fasting insulin and HOMA-IR in the overall population ($p\text{-trend} < 0.01$ across quartiles of phthalate metabolites). These positive associations were also observed in gender and racial subgroups, with Mexican-Americans and non-Hispanic blacks having modestly stronger dose-response relationships compared to non-Hispanic whites [e.g., the median increases of FBG for those in the highest versus lowest quartiles of ΣDEHP were 5.48 (95% CI: 3.06, 7.90), 2.32 (95% CI: 0.12, 4.52) and 0.94 (95% CI: -1.10, 2.98) mg/dL, respectively]. However, no difference was noted between men and women. These findings require further investigation, but could suggest that Mexican-Americans and non-Hispanic blacks may be more vulnerable to phthalates with respect to glucose homeostasis, resulting in higher diabetes prevalence in these groups.

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SNP INTERACTIONS IN GWAS IDENTIFIES NOVEL DISEASE SUSCEPTIBILITY LOCI – THE WTCCC DATA REVISITED.

*Noha Sharaf Eldin, Qi Liu, Shahab Jabbari, Linwei Wang, Conrado Franco-Villabos, Surakameth Mahasirimongkol, Hideki Yanai Yanai, Katsushi Tokunaga, Yutaka Yasui (University of Alberta, Edmonton AB Canada)

Objectives: Genome wide association studies (GWAS) examine single nucleotide polymorphisms (SNPs) associated with disease risk. A single-SNP analysis ignores combined effects of multiple SNPs. Reported odds ratios are small despite their high statistical significance, thus of minimal clinical/public health significance. We aimed to further identify disease susceptibility through exploring SNP-SNP interactions. Methods: We re-analyzed The Wellcome Trust Case Control Consortium[1] (WTCCC) data examining two biologically plausible SNP-SNP interactions: SNP *intersection* and SNP *union*. SNP-SNP interactions were searched for within each gene using logic regression.[2] We examined an average of 221,049 SNPs over 13,093 genes in association with six diseases: bipolar disorder (BD), coronary artery disease (CAD), hypertension (HT), rheumatoid arthritis (RA), type 2 diabetes (T2D), and type 1 diabetes (T1D). A Corrected-Bayes Factor (C-BF) was used as a measure of evidence of association and a BF threshold indicating strong evidence of association of a gene with a disease was calculated for each disease. P-value for each gene was calculated by permutation tests. Results: The BF threshold was 4.12 for the six diseases examined in this analysis. The number of genes showing strong evidence of association was: 411 for BD, 290 for CAD, 301 for HT, 362 for RA, 266 for T2D and 330 for T1D. All strong signals reported from the WTCCC single-SNP analysis were replicated in our analysis. In addition, strong evidence emerged implicating new genes that are backed up with apparent biological links to disease. Among the top significant genes were: *CBLN4* with BD, *P2RX4* with CAD, *BBOX1* with HT, *STAG3L4* with RA, and *RHOJ* with T2D. Conclusion: Novel disease susceptibility loci with biologically plausible links to six diseases were detected in our interaction analysis. This emphasizes the importance of searching for SNP-SNP interactions in addition to the standard single-SNP analysis in GWAS. References 1.Wellcome Trust Case Control Consortium. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Nature 447, 661-678 (2007). 2.Ruczinski, I., Kooperberg, C. & LeBlanc, M. Logic Regression. Journal of Computational and Graphical Statistics 12, 475-511 (2003).

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A GENOME-WIDE ASSOCIATION STUDY OF COGNITIVE DECLINE SHOWS TWO INDEPENDENT SIGNALS IN THE APOE/TOMM40 REGION. *Chenan Zhang, Brandon Pierce (University of Chicago, Chicago IL 60615)

Background: Age-related cognitive decline is a major public health concern facing the large segment of the U.S. population approaching retirement. Identifying the genetic risk factors related to cognitive decline is crucial for understanding its onset and progression, and for developing intervention strategies. Methods: The Health and Retirement Study (HRS) is a longitudinal study involving >26,000 Americans over the age of 50, and data is publicly available. HRS collects phenotype data every two years, including cognitive measures. Genotype data is available for >12,000 participants, consisting of >1.6 million single nucleotide polymorphisms (SNPs). A mixed effects model was used to estimate individual trajectories of cognitive decline for participants with at least two observations after age 65. A genome-wide association study (GWAS) of this phenotype was conducted, with separate analyses for participants of predominantly European ancestry (n = 5822) and participants of substantial African ancestry (n = 918). Results: In the analysis of European Americans, the SNP with the most significant association was rs769449 ($P = 3.141 \times 10^{-13}$), located in an intronic region of the APOE (apolipoprotein E) gene on chromosome 19. In analyses conditioned on the APOE SNP, an additional SNP in this region, located in the TOMM40 (translocase of the outer mitochondrial membrane 40 homolog) gene demonstrated a genome-wide significant association ($P = 2.53 \times 10^{-9}$). In the analysis of African Americans, there was no evidence of APOE nor TOMM40 being associated with cognitive decline. Conclusion: While variants in the APOE/TOMM40 region have previously been implicated in cognitive decline, this is the first GWAS with evidence of two independent association signals. Furthermore, this is the first reported cognitive decline GWAS of African Americans, with evidence that SNPs in this region do not confer comparable risks in this group.

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GENOME-WIDE ASSOCIATION, CANDIDATE GENE, AND PATHWAY ANALYSIS STUDIES OF PLACENTAL ABRUPTION. *Tsegaselassie Workalemahu, Daniel Enquobahrie, Sixto Sanchez, Cande Ananth, Percy Pacora, Liming Liang, Michelle Williams (Harvard School of Public Health, Boston MA 02115)

Background: Placental abruption (PA), a leading cause of maternal and perinatal mortality, is a pregnancy-related vascular disorder. The success of identifying susceptibility loci for PA, a complex multi-factorial disease with high heritability, has been limited. Methods: We conducted a genome-wide association study (GWAS) using 470 PA cases and 473 controls from Lima, Peru. We also performed a candidate gene association study to evaluate the extent to which variations in 35 genes that participate in mitochondrial biogenesis (MB) and oxidative phosphorylation (OP) influence PA risk. Variants in cardiovascular and metabolism genes, across the genome, were characterized using ~125,000 single nucleotide polymorphisms (SNPs) on the Illumina Cardio-Metabo Chip. We examined functions and functional relationships of genes represented by the top 200 hits from our GWAS using pathway-based analyses exploring joint effects of gene sets within specific pathways. Results: The top hit in our GWAS study was rs1238566 (p-value = 1.04e-4) in FLI-1 gene, a megakaryocyte-specific transcription factor. In pathway analyses of 51 genes represented by the top 200 GWAS hits (p-values < 2.1e-3), leading networks were enriched by genes involved in lipid metabolism (e.g., FLI-1, CETP, LIPC, and THRB) and cell signaling (e.g., Akt, NFKB, and PI3K). In candidate gene analyses, SNPs in genes in MB (e.g. CAMK2B, NR1H3, PPARG, PRKCA, and THRB) or OP (e.g., COX5A, and NDUF family of genes) pathways were significantly associated with PA. Conclusion: Integrating different genomic analytical strategies provides opportunities for identifying novel biological pathways for exploring underlying molecular mechanisms for PA.

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COMMON MARKERS IDENTIFIED BY SEQUENCING CASE-PARENT TRIOS CONFIRMS 8Q24 CONTAINS A GENETIC RISK FACTOR FOR CLEFT LIP WITH/WITHOUT CLEFT PALATE WITH SUBSTANTIAL HETEROGENEITY ACROSS POPULATIONS. Elizabeth Leslie, Samuel Younkin, Mary Marazita, Azeez Butali, Andrew Lidral, Alan Scott, Ingo Ruczinski, Margaret Taub, Jacqueline Hetmanski, Margaret Parker, Hang Wang, David Larson, Christopher Harris, Daniel Koboldt, Karyn Steinberg, George Weinstock, Jeffery Murray, *Terri Beaty (Johns Hopkins University, Dept of Epidemiology, Baltimore MD 21205)

Evidence for a genetic factor controlling risk to cleft lip with/without cleft palate (CL/P) in the chromosome 8q24 region has been seen in case-control studies and case-parent trio studies. We undertook a targeted sequencing study to closely examine an approximately 1Mb region on 8q24 in 1,289 CL/P case-parent trios from three populations (320 trios of European ancestry, 588 trios from the Philippines and 381 Chinese trios). We identified 25,168 variants in this region, including 3,256 with minor allele frequency (MAF) > 0.01 and 21,912 low frequency and rare variants. We used the common SNPs (MAF > 0.01) in a transmission disequilibrium test (TDT) for linkage and association in the total sample and stratified by population. Evidence of linkage and association was strongest among trios of European ancestry (yielding $10^{-10} > p > 10^{-11}$), but these same markers were less significant among Chinese and Filipino trios ($p > 10^{-4}$). Part of this difference in statistical significance reflects variation in heterozygosity levels at markers among the three populations, where individual SNPs had higher MAF among European parents compared to Filipino and Chinese parents. Haplotype analysis within groups also showed considerable variation over a 159kb region flanking rs987525, the original SNP reported to be a significant genetic risk factor for CL/P. Natural variation in MAF (and heterozygosity) plays an important role in the ability to detect common variants influencing risk to CL/P using case-parent trios from different populations. Rare variants will also be incorporated into these tests.

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52 ESTABLISHED MULTIPLE SCLEROSIS RISK LOCI ARE NOT ASSOCIATED WITH DISEASE SEVERITY IN A META-ANALYSIS OF 3,056 CASES. *Michaela F George, Farren B. S Briggs, Xiaorong Shao, Hanne F Harbo, Ellen Mowry, Hong Quach, Brigid Acuna, Ling Shen, Allan Bernstein, Cathy Schaefer, Lisa F Barcellos (Division of Epidemiology, School of Public Health, University of California, Berkeley CA 94720)

Multiple sclerosis (MS) is an autoimmune disease affecting the central nervous system with genetic and environmental hypothesized predictors of disease progression. MS progression is heterogeneous, with varying manifestations in cognitive and physical systems. We hypothesize that MS risk variants may also predict disease progression. We investigated the effect of 52 risk loci identified from the largest genome-wide association study (GWAS) in MS (Nature 2011) and the combined weighted genetic risk score (wGRS) on three clinical phenotypes: Multiple Sclerosis Severity Score (MSSS), cognitive status, and site of first symptom in 1,008 non-Hispanic White MS patients identified from a large MS registry within Kaiser Permanente Medical Care Plan – Northern California. We calculated wGRS by combining the natural log of odds ratios from the 52 independent risk loci from the largest MS GWAS ($N \approx 30{,}000$). MSSS was calculated for each case using the Expanded Disability Status Scale at study entry and disease duration. Cognitive score for each case was determined using a validated telephone interview cognitive status assessment tool. Site of first symptom was defined as the neurological system affected for three days or more, leading to a diagnosis of MS. In our population of MS cases there were no significant relationships between individual risk variants or wGRS and any of the three clinical phenotypes. We confirmed the null association for MSSS in a meta-analysis of four independent data sets (Norway, San Francisco, Boston, United Kingdom), for both wGRS and 52 risk loci. This is the first study to investigate the effect of wGRS and all established MS risk loci on clinical phenotypes, and also the largest study to investigate MSSS among MS cases. Based on these results, we conclude that the genetic mechanisms of MS progression are different than MS onset; and perhaps environmental factors are more important for progression and have yet to be discovered.

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CANDIDATE VITAMIN D RISK VARIANTS FROM A LARGE GENOME-WIDE ASSOCIATION STUDY ARE NOT ASSOCIATED WITH MULTIPLE SCLEROSIS PROGRESSION. *Farren B. S Briggs, Michaela F George, Ellen Mowry, Xiaorong Shao, Hong Quach, Brigid Acuna, Ling Shen, Allan Bernstein, Cathy Schaefer, Lisa F Barcellos (Division of Epidemiology, School of Public Health, University of California, Berkeley CA 94720)

Multiple sclerosis (MS) is an autoimmune disease affecting the central nervous system with both genetic and environmental hypothesized predictors of disease progression. The progression of MS is heterogeneous, with differential manifestations in both cognitive and physical systems. Vitamin D has been shown to have protective effects on the onset and progression of MS. We investigated the effect of functional variants of vitamin D metabolism genes on several measures of progression in 1,008 non-Hispanic White MS patients identified in a large registry within the Kaiser Permanente Medical Care Plan - Northern California. Of the 15 vitamin D candidate genes known to be involved with metabolism, we identified 65 functional single nucleotide polymorphisms (SNPs) within our dataset, 42 of which met quality control measures. We investigated three clinical outcomes or progression phenotypes: site of first symptom, cognitive status, and Multiple Sclerosis Severity Score (MSSS). Site of first symptom was defined as the neurological system affected for three days or more and is considered the onset of symptoms leading to a diagnosis of MS. Cognitive score was determined from a validated telephone interview cognitive status assessment tool. MSSS was calculated for each case using the Expanded Disability Status Scale at study entry and disease duration. In our population of MS cases, there were no significant associations between the vitamin D functional variants and any of the clinical phenotypes. This is among the first studies to investigate the effect of functional variants in vitamin D candidate genes on important MS phenotypes. Other studies have shown that vitamin D has a protective effect on MS progression; however the functional variants in vitamin D metabolism genes are not responsible for that protection. Perhaps there are gene by environment interactions that may help explain genetic involvement in progression of MS.

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ELECTRONIC MEDICAL RECORDS AND GENOMICS NETWORK – FROM GWAS TO IMPLEMENTATION. *Ian Marpuri, Erwin P Bottinger, Murray H Brilliant, David Carey, Rex L Chisholm, Christopher G Chute, Jonathan L Haines, Hakon Hakonarson, John Harley, Gail P Jarvik, Isaac Kohane, Iftikhar Kullo, Eric B Larson, Catherine McCarty, Dan Roden, Maureen Smith, Marc S Williams, Rongling Li (National Human Genome Research Institute/NIH, Bethesda MD)

The eMERGE (Electronic Medical Records and Genomics) Network is a consortium funded by the National Human Genome Research Institute to investigate the use of electronic medical records (EMRs) and biorepositories in genomic research (Phase I, 2007-2011) and the incorporation of genomic variants into EMRs for use in clinical care (Phase II, 2011-2014). eMERGE had five study sites in Phase I and now has nine study sites and a Coordinating Center in Phase II. Phase I sites conducted genome-wide association studies (GWAs) for 13 phenotypes on ~19,000 genotyped participants. The Network published GWAs on LDL cholesterol, monocyte count, red blood cell traits, type 2 diabetes, white blood cell count, and hypothyroidism. These Network GWAs identified 12 novel loci and replicated 16 loci. In Phase II, the Network plans to conduct GWAs for 24 additional phenotypes on a total of ~87,000 genotyped participants. Lessons learned in Phase I include design of robust algorithms for EMR-based phenotyping that are transportable across different EMRs and data types, protocols for return of incidental findings, phenome-wide analysis of variants based on ICD9 codes, and model consent language to better inform participants in genomics research. Goals in Phase II include defining standards for clinical validity and actionability, sharing executable phenotype definitions, creating standards for sharing CLIA certified results with EMRs, representing linked genotype-phenotype data in EMRs, and consulting with health care practitioners and patients about return of results. Implementation projects include genomic risk scores, measures of clinical utility and physician uptake of alerts, and a Network pilot study implementing specific pharmacogenetic variants in EMRs.eMERGE's collaborations within and outside the Network and its large, diverse group of genotyped participants linked to EMRs make it a suitable arena to test the feasibility of using genomic data in clinical care.

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ADH1B (RS1229984) AND DSM-IV ALCOHOL ABUSE & DEPENDENCE CRITERIA, WITH ALCOHOL CONSUMPTION AS MEDIATOR IN ISRAELI DRINKERS. *Bari Kilcoyne, Dvora Shmulewitz, Efrat Aharonovich, Howard Edenberg, Joel Gelernter, Deborah Hasin (Columbia University, New York NY 10037)

Introduction: A single-nucleotide polymorphism (SNP) in the *ADH1B* gene, rs1229984, leads to a functional change in the ADH1B alcohol dehydrogenase enzyme. The protective allele produces an enzyme with faster acetaldehyde production. This is associated with lower alcohol consumption (maximum drinks in 24 hours; Maxdrinks) and lower risk for alcohol use disorders (AUDs). While DSM-IV AUDs are diagnosed using 11 different criteria, the association between ADH1B and each individual AUD criterion is unknown and was therefore investigated in this study. Further, based on the premise that faster ADH1B kinetics lead to decreased drinking, we formally tested Maxdrinks as a mediator of the relationship between *ADH1B* and the individual AUD criteria. Methods: Analysis included 1,130 lifetime drinkers from a household sample in Israel, assessed with a structured interview and genotyped for rs1229984 (MAF = 0.28). Associations between *ADH1B* and each DSM-IV criterion were analyzed using logistic regression. For criteria significantly related to ADH1B, mediation by Maxdrinks was tested with logistic regression and bootstrapping. Results: *ADH1B* was significantly associated with 6 criteria, with odds ratios (ORs) ranging from 1.32 to 1.96, e.g., the dependence criterion larger/longer (*drinking more or over longer periods than intended*; OR = 1.75). Maxdrinks was a significant mediator of these relationships, explaining a substantial proportion of the associations, e.g., 35% of the total *ADH1B* effect on larger/longer. Conclusion: This is the first study to examine the relationship of *ADH1B**rs1229984 to specific DSM-IV criteria, finding that 6 of the 11 were related, and to show that alcohol consumption explained a significant proportion of these associations. A deeper understanding of the associations between *ADH1B* and the DSM-IV AUD criteria, including indirect effects through consumption, will enhance our understanding of the etiologic model through which AUDs occur.

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THE MISMEASUREMENT OF QUALITY BY READMISSION RATE. HOW BLUNT IS TOO BLUNT AN INSTRUMENT. *Juliet Rumball-Smith, Tony Blakely, Diana Sarfati, Phil Hider (University of McGill, Montreal QC Canada)

The rate of readmission is widely used as a measure of hospital quality of care, with some jurisdictions financially penalizing facilities deemed to have excessive rates. Motivated by evidence of racial disparities in healthcare and ethnic inequalities in health status, we compared healthcare quality for Maori (the indigenous people of New Zealand) and Europeans using readmission. In a sample of 89,090 surgical patients, Maori had a 16% higher readmission rate (odds ratio 1.16, 95% confidence interval 1.08 – 1.24). But how sure can we be that this estimate truly represents poorer quality of care for Maori? We applied a structural Directed Acyclic Graph framework and performed quantitative bias analyses, to explore the plausibility of readmission as a proxy for healthcare quality in this context. Ethnicity was defined as the exposure, the rate of readmission as the proxy outcome, and quality of care as a missing mediator. Using our data and estimates from the literature of the prevalence of 'poor quality' and the strength of the quality of care-readmission association, a series of sensitivity analyses were performed to calculate an odds ratio of the ethnicity-readmission association corrected for the missing mediator 'quality'. Given our assumptions, an unfeasibly strong ethnicity-quality association, or an implausibly strong quality-readmission association, would be necessary to 'explain away' the residual association of ethnicity with readmission. Overall, we estimated that potentially only 29% of the ethnicity-readmission association was due to inpatient quality of care. We conclude there is substantial error when using readmission as a marker of quality, and suggest that differences in readmission between populations are more likely to be due to factors other than quality of care.

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EXTENDED CAUSAL DIAGRAMS INTEGRATING RESPONSE TYPES AND OBSERVED VARIABLES. *Etsuji Suzuki, Toshiharu Mitsuhashi, Toshihide Tsuda, Eiji Yamamoto (Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan)

The counterfactual approach provides a clear and coherent framework to think about a variety of important concepts related to causation. In this approach, individuals can be classified by the patterns of their potential outcomes, which are often referred to as response types. Meanwhile, directed acyclic graphs (DAGs) have long been used as causal diagrams in epidemiologic research to visually summarize hypothetical relations among variables of interest. DAGs have been used extensively to determine the variables for which it is necessary to control for confounding bias to estimate causal effects. Besides, various types of selection bias have been shown to share a common underlying causal structure, and conditioning on common effects is now referred to as selection bias. In this study, we attempt to explain the concepts of confounding bias and selection bias by extending causal diagrams, which integrate response types and observed variables. By so doing, we can describe how the observed variables are determined in response to the corresponding response types and their measured parent(s). To demonstrate their benefits, we show three extended causal diagrams, or extended DAGs, depicting (1) a hypothetical situation under marginal randomization; (2) a hypothetical situation under stratified randomization; and (3) a hypothetical situation in observational studies. Although these extended DAGs may appear less intuitive, they maintain the integrity of the original DAGs and we can apply the rule used in the standard DAG theory. Extended DAGs would be of great use in graphically describing the sufficient conditions to estimate effect measures in observational studies.

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THE CASE TEST-NEGATIVE DESIGN FOR VACCINE EFFECTIVENESS AGAINST HOSPITALIZATION. *Ivo Foppa, Jill Ferdinand, Sue Reynolds (Centers for Disease Control and Prevention; Battelle Memorial Institute, Atlanta GA 30329)

The so-called "test-negative case-control" study design (TND) is popular for the assessment of the effectiveness of seasonal influenza vaccination. According to this design cases are chosen among individuals presenting to medical care for acute respiratory illness and who test positive for an influenza virus, while controls are individuals who present similarly and test negative for influenza. We have shown previously that, under a broad set of assumptions, this design gives rise to unbiased estimates of vaccine effectiveness (VE) when applied in an outpatient setting, using a highly sensitive and specific diagnostic test. Here, we examine the properties of VE estimates derived from a TND in which cases and test-negative controls are chosen among individuals hospitalized for acute respiratory illness. A theoretical derivation of the properties of VE estimates derived from a study of that design is followed by a simulation study. We describe the conditions under which the resulting estimates of VE against influenza-associated hospitalization are biased and propose measures to avoid bias.

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UNDERSTANDING THE ASSOCIATION OF HARMFUL RISK FACTORS AND LOWER MORTALITY AMONG THOSE WITH DISEASE: ILLUSTRATED WITH OBESITY AND END-STAGE RENAL DISEASE. *William Flanders, William McClellan (Emory University, Atlanta GA 30345)

Introduction: Risk factors suspected of causing certain chronic diseases and mortality are often associated with lower mortality among the diseased. For end-stage renal disease (ESRD), examples include high cholesterol, blood pressure, homocysteine, and creatinine. We illustrate the phenomenon using obesity which is thought to cause both ESRD and premature mortality, yet is associated with lower mortality among ESRD patients. Methods: These associations reflect causal issues, and so we carefully define causal effects and use potential-outcome models that incorporate our causal assumptions to characterize the observed associations that can arise. Using potential outcome models, we identify a mechanism for bias related to competing risks. We also show that the lower mortality can arise absent bias, even if obesity has only harmful effects on risk of ESRD and death. Results: Through examples, we illustrate how plausible patterns of only harmful causal effects can lead to an association of obesity with lower mortality, once ESRD has occurred usual. Other examples illustrate how competing risks can bias effect estimates. This bias differs from structural selection and other biases previously proposed, although these other biases can contribute as well. We also illustrate a method of analysis that avoids the bias due to competing risks. Conclusion: We illustrate using obesity, ESRD and mortality, but our conclusions apply more generally. For example, similar 'paradoxical' associations are commonly observed between obesity and cardiovascular diseases like congestive heart failure.

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SENSITIVITY AND SPECIFICITY ON SEMI-HEALTH CONDITIONS AMONG YOUNG ADULTS IN JAPAN. *Hideo Yamazaki (Hamamatsu University, Hamamatsu Shizuoka Japan)

Introduction: The purpose of the present study was to indicate a cutoff point based on the semi-health index, which indicated a level of transitional condition on one's health, and to clarify sensitivity and specificity of semi-health symptoms among young adults in Japan. In Japan, chronic diseases such as metabolic syndrome are called life-style related diseases. They are not only serious causes of death but also risk factors of broken health. Health problems caused by circulatory diseases have been steadily increasing. It is noted that the preventive measures should be taken from a relatively early stage in one's life. Methods: The self-report questionnaire, which consisted of 53 items, was administered to 2,074 young adults in Japan between 2011 and 2012. Then a principal components analysis was applied to the valid data in order to extract indices which represented structural characteristics on semi-health condition. Results: By the principal component analysis, four principal components were extracted. Especially, the first principal component was extracted as an index which indicated a quantitative aspect of the semi-health condition. Every eigenvector of its component had a mark of plus. In this study, therefore, this component was used as the semi-health index. Furthermore, a distribution of young adults with semi-health symptoms in Japan was determined by using the semi-health index. Then a cutoff point was calculated from the value of the index in order to determine predictive value of discriminating the semi-health from good health condition. Finally, the sensitivity (89.0%) and specificity (84.2%) were derived form the distribution based on the semi-health criterion.

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CUMULATIVE DISTRIBUTION FUNCTIONS AS A SIMPLE METHOD TO DEFINE LOST TO FOLLOW-UP (LTFU) CUT-OFFS AMONG PATIENTS INITIATED ON ANTIRETROVIRAL THERAPY (ART) IN ZOMBA, MALAWI. *Beth Rachlis, Michael Escobar, Donald C Cole (University of Toronto, Toronto ON Canada)

Background: Operational definitions of LTFU vary widely making comparisons across ART programmes challenging. Definitions should be evidence-based and simple to calculate so that they can be applied by programme planners with limited statistical expertise working in resource- constrained settings. Current methods have relied on fixed time period cohort approaches. We applied Cumulative Distribution Functions (CDFs) as a novel method to define a LTFU cut-off. Methods: Patients who initiated ART with Dignitas International supported sites in Zomba, Malawi between January 1 2007-June 30 2010 were eligible for inclusion. Lateness was categorized using 7-day cut-offs from ≥7 to ≥182 days late. At each cut-off, we identified the proportion of patients who returned for a subsequent visit within 12 months of an expected visit. CDFs were plotted to determine the probability of returning within 12 months as a function of lateness. CDFs were also plotted for potential predictors of LTFU and were visually examined to determine the cut-off after which the probability of a returning decreases. Results: In total, n = 4484 patients with n = 7316 visits were included. CDFs demonstrated that the proportion of patients who subsequently returned within 12 months increases sharply up to 42 days late. The curve then increases more gradually up until the 56 days late cut-off and then begins to flatten out suggesting that the proportion of patients who return for a subsequent visit decreases once a patient is between 42 -56 days late for a visit. CDFs plotted for potential predictors of LTFU demonstrated similar patterns. Discussion: CDFs are a simple method for determining LTFU cut-offs. Plotting CDFs requires little statistical expertise and can be done using basic computer software making it a practical method for HIV programmes in resource- constrained settings. Our finding of a LTFU cut-off ranging from 42-56 days late is consistent with previous literature.

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CONSIDERATIONS IN POOLING BIOMARKER CALIBRATION INFORMATION. *Neil Perkins, Sunni Mumford, Enrique Schisterman (Eunice Kennedy Shriver National Institute of Child Health and Human Development, Rockville MD 20852)

Biomarker assays often consist of a two stage process where laboratory equipment yields a relative measure which is subsequently transformed to the unit of interest using a calibration experiment. The calibration experiment uses stepped samples of known biomarker levels to establish the relation between the measured relative units and sample biomarker levels. Samples are often measured in multiple batches or plates, each with independent standard calibration. Collapsing calibration information across batches has been shown to reduce measurement error and improve estimation of parameters of interest. However, collapsing in practice can also create an additional layer of quality control and optimization in a part of the laboratory measurement process that is often highly automated. Here we use real data to motivate and display the benefits of collapsing calibration experiments such as detecting and overcoming faulty calibration experiments and reducing the need for rerunning out of range samples. Leptin and AMH were measured using ELISA in 3876 samples across 53 batches from biospecimens from the BioCycle study of hormonal variability. The laboratory used both cubic splines and linear cubic regression for batch-specific calibration, and these same techniques were employed when collapsing calibration experiments. Collapsing calibration experiments reduced variability as well as enabled measurement of 78 AMH values that would have been missing as out of range. These simple and practical procedures are minor adjustments implemented by study personnel without altering laboratory protocols which could have positive estimation and cost savings implications especially for population based studies.

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MULTIPLY ROBUST ESTIMATION OF EFFECTS IN CASE CONTROL STUDIES IN THE PRESENCE OF SELECTION BIAS. *Maral DerSarkissian, Onyebuchi A Arah (Department of Epidemiology, University of California Los Angeles Fielding School of Public Health, Los Angeles CA 90095)

Selection bias is especially problematic when both the exposure and outcome affect study participation in case control studies. Even though epidemiologists go to great lengths to avoid such bias, it can still creep into studies. When faced with this type of Berskonian bias, investigators can conduct sensitivity analysis using inverse probability of selection weighting or the bias breaking variable method. In case control studies suffering from Berksonian bias, multiply robust estimation, which combines three or more estimators (or sub-models) in a single union model, offers investigators a combined tool for bias analysis and confounding control to protect against model misspecification. For instance, investigators using the multiply robust approach may use inverse probability of selection weights to adjust for selection bias, and propensity score covariate adjustment and outcome regression to have two chances for correct specification of confounding control. We used Monte Carlo methods to examine the effect of a binary exposure on a binary outcome in the presence of selection bias and multiple confounders in case control studies. We examined the performance of multiply robust estimation under different model specification scenarios using inverse probability of selection weighted fitting of marginal structural models, propensity score covariate adjustment, and outcome regression to build union models. We evaluated bias, variance, and confidence interval coverage. Our results showed that odds ratios were unbiased in all scenarios where (1) inverse probability of selection weights were correctly specified and at least one sub-model was correctly specified for confounding control, or (2) at least one sub-model was correctly specified for confounding control and inverse probability of selection weights were misspecified but at least one sub-model included the omitted selection-inducing variable if it was on a backdoor path.

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NON-DIFFERENTIAL MISCLASSIFICATION IN AGGREGATED MEASURES OF NEIGHBORHOOD CONTEXT. *Stephen Mooney, Catherine Richards, Andrew Rundle (Columbia University Mailman School of Public Health, New York NY 10025)

Background: Studies of incorporating neighborhood characteristics as predictors frequently aggregate individual level data to create contextual measures. For example, percent of residents in poverty is an aggregation of individual-level measurements of household size and household income, both measures likely to include error. We explored the bias introduced by non-differential misclassification in individual-level data aggregated for use as a contextual measure. Methods: We conducted simulation studies using GEE and mixed models to relate neighborhood contextual measures derived from Census data to an individual level outcome variable, varying the extent of non-differential misclassification in the underlying Census measures. We assessed the consequences of misclassification on neighborhood effect estimates. Results: For neighborhood variables aggregated from dichotomous measures (e.g. % of residents living below the poverty line), non-differential misclassification at the individual level inflates the associated regression parameter estimate to 1/(sensitivity + specificity-1) times the true value in both GEE and mixed models. However, no bias is present in comparisons between rank-ordered neighborhoods (e.g. comparing quartiles of neighborhoods by percent of residents in poverty). Comparisons of neighborhoods grouped by external cutpoints (e.g. neighborhoods with <5% of residents in poverty vs. neighborhoods with >20% of residents in poverty) may be biased towards or away from the null, though bias away from the null is more frequent. Discussion: When using contextual measures created through the aggregation of individual level data, the effect of non-differential misclassification at the individual level depends on the comparison estimated. No bias is present in estimates interpreted as the average difference in outcome between quantiles of neighborhoods.

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A NOVEL NETWORK GRAPH APPROACH FOR THE ANALYSIS AND VISUALISATION OF EPIDEMIOLOGICAL DATA.

*Gemma Sharp, Tom Freeman, Philippa Saunders, Jane Norman (Centre for Reproductive Health, University of Edinburgh, Edinburgh United Kingdom)

Background: Conventional data analysis in epidemiology relies on testing hypotheses generated by the researcher. Although undoubtedly useful, this approach risks overlooking interesting and confounding associations the researcher does not expect to see. We propose a new method to generate hypotheses in an unbiased manner. Methods: Using *BioLayout Express3D* (most commonly used to analyse gene expression data) we build three dimensional network graphs where each *node* represents a risk factor or outcome, connected by *edges* whose lengths are determined by the strength of the correlation. Markov chain cluster analysis identifies groups of highly correlated factors that appear to be interrelated. These clusters are used to generate hypotheses about associations that can be tested using more conventional univariate and multivariate analyses. Results: We evaluated the technique by building network graphs of data from The Walker Project, a database of 32234 birth records collected from 1952-1968. Risk factors and confounding variables clustered with certain clinical outcomes, and these clusters predicted the results of univariate and multivariate regression analyses. A main strength of this approach is the ability to cope well with missing data. For example, delivery by Caesarean section clustered with previous Caesarean delivery, pelvic deformities, cephalo-pelvic disproportion, maternal tumours and abnormal fetal presentation. These were confirmed as important risk factors in univariate analyses (odds ratios ranging 5.4 to 115.9; 95% confidence intervals ranging 2.5 to 165.5), but there were too few complete cases to fit a regression model, which relies more heavily on complete data. Conclusion: Network graphs are a quick and informative new method to visualise and analyse epidemiological data in an unbiased manner. The approach copes well with missing data, making it a useful complementary method to conventional analyses.

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CONTROLLING FOR THE HEALTHY WORKER SURVIVOR BIAS WITH G-ESTIMATION OF ACCELERATED FAILURE TIME MODELS USING A SERIES OF EXPOSURE CUTOFFS: A MOVE TOWARD QUANTITATIVE EXPOSURE.

*Sally Picciotto, Jonathan Chevrier, Ellen A Eisen (University of California, Berkeley: School of Public Health, Berkeley CA 94720)

Background: To prevent healthy worker survivor bias, g-estimation of an accelerated failure time model is a good analytic method for occupational cohorts with longitudinal exposure data. However, technical challenges make the method difficult to implement with quantitative exposures. Methods: We used several binary exposure measures, each representing an annual average daily exposure above vs. below a series of cutoffs, to assess the potential impacts of exposure interventions. We applied the method to a study of exposure to PM3.5 composed of metalworking fluid and chronic obstructive pulmonary disease (COPD) mortality in a large cohort of autoworkers. For each cutoff, we used g-estimation to calculate the population mean of the counterfactual years of life saved under an intervention in which annual exposure was not permitted to exceed the cutoff. The years of life saved for each intervention were computed relative to the observed outcomes, which were common to all cutoffs. Because the effect measure in each analysis relates counterfactual outcomes under an intervention to observed outcomes under no intervention, results from the different cutoffs may be compared. Results: Beginning with a cutoff of 0.15mg/m3, the impact of the intervention progressively increased as the cutoff approached 0. For example, the interventions that allowed no one to be exposed above 0.15, 0.10, and 0.05mg/m3 would have saved each COPD case a mean (standard deviation) of 0.1 (0.4), 0.7 (1.9), and 0.6 (1.6) years of life, respectively. The greatest impact was observed for a cutoff of 0—in other words, for the most extreme intervention, in which nobody is ever exposed: in that case, a mean of 1.5 (2.4) years of life would have been saved for each COPD case. Conclusion: This method allows for a comparison of the impacts of hypothetical interventions limiting workplace exposures to below various levels.

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COMPETING RISK VERSUS KAPLAN-MEIER ANALYSIS FOR ESTIMATING LOSS TO FOLLOW-UP IN HIV PROGRAMS.

*Chloe A Teasdale, Matthew Lamb, Harriet Nuwagaba-Biribonwoha, Elaine J Abrams, Chunhui Wang (Department of Epidemiology & ICAP, Mailman School of Public Health, Columbia University, New York NY 10032)

Background: Retention of HIV+ patients prior to initiation of anti-retroviral therapy (ART) is important for ensuring timely ART initiation but pre-ART loss to follow-up is a common challenge for HIV service programs. Kaplan-Meier (KM) estimators are often used to assess rates of loss to follow-up however they do not account for the competing risks of death and ART initiation. Competing risk (CR) approaches are an alternative method for analyzing time-to-event data which account for informative censoring from events which preclude the outcome of interest. We used data from a large cohort of adults enrolled in HIV care in Rwanda to compare these methods for assessing loss to follow-up. Methods: We analyzed routinely-collected data on HIV+ adults >15 years enrolled at 41 healthcare facilities in Rwanda from 2004 to 2010. Cumulative incidence of loss to follow-up (not attending clinic in the last 12 months) in patients prior to ART initiation at 1 and 3 years after enrollment was estimated using KM and CR methods. Results: A total of 31,390 ART-naïve adults were included in the analysis, of whom, 17,569 (56%) initiated ART. KM and CR estimates of loss to follow-up differed at all time points. At 1year after enrollment, cumulative incidence of loss to follow-up was 13.5% (95% CI 13.0-14.0%) using KM compared to 8.7% (95% CI 8.4-9.1%) using CR. At 3 years after enrollment, 22.3% (95% CI 21.7-23.1%) of patients were estimated to be loss to follow-up using KM compared to 12.7% (95% CI 12.3-13.2%) using CR. Conclusions: Loss to follow-up among pre-ART patients in Rwanda was overestimated using KM methods which did not consider death and ART initiation as competing risks. These results show the importance of considering informative censoring in survival analyses.

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QUANTITATIVE VERIFICATION OF INSTRUMENTAL VARIABLES ASSUMPTION USING BALANCE MEASURES.

M Jamal Uddin, **M Sanni Ali, *Rolf HH Groenwold, W. R Pestman, Svetlana V Belitser, Arno W Hoes, Anthonius de Boer, Kit CB Roes, Olaf H Klungel (Both authors contributed equally, University of Utrecht, Utrecht Netherlands)

Background: Instrumental variable (IV) analysis appears to be an attractive method to adjust for confounding in non-randomized studies. One of the underlying assumptions is that the IV is independent of confounders. If this assumption is violated, the IV estimate can be severely biased. Methods: We conducted Monte Carlo simulations to assess the performance of balance measures commonly used in propensity score methods (in particular, the standardized difference) to verify this assumption quantitatively. We simulated cohorts of varying sample sizes, binary IV and exposure, continuous outcome, and several confounders. Different associations among IV, exposure, and confounders were considered and 10,000 replications were used in each scenario. Data were analyzed using the two-stage least square method. The balance of confounders across IV levels was assessed using the standardized difference. Values of the standardized difference that are close to zero indicate a balance of confounders across IV groups. We also estimated the correlation between the standardized difference and bias of the IV estimates. Results: Bias of IV estimates increased with weaker IVs (i.e., weak association between IV and exposure) and increasing values of the standardized difference (i.e. decreasing balance of confounders across IV categories). IV estimates were more biased than those of classical regression estimates with increasing values of the standardized difference, and a weak IV amplified this bias. Conclusions: Balance measures that are commonly used in propensity score methods can be useful tools to quantitatively verify one of the assumptions underlying IV analysis, i.e., that the IV should be independent of confounders. However, these balance measures only quantify the balance of observed confounders and not of unobserved confounders.

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A SIMULATION STUDY OF RELATIVE EFFICIENCY AND BIAS IN THE NESTED CASE-CONTROL STUDY DESIGN. *Stephen Bertke, Misty Hein, Mary Schubauer-Berigan, James Deddens (Centers for Disease Control and Prevention, Cincinnati OH 45226)

Purpose: The nested case-control study design, in which a fixed number of controls are matched to each case, is often used to analyze exposure-response associations within a cohort. It has become common practice to sample 5 – 10 controls per case, however, previous research has shown that in certain instances, significant gains in relative efficiency can be realized when more controls are matched with each case. This study expanded upon these results through a simulation study by also considering a continuous exposure variable as well as investigating potential bias due to small sample sizes. Methods: A simulation study was conducted investigating the effect of the number of cases, strength of exposure-response relation and skewness of exposure variable on bias and relative efficiency. Results: It was shown that relative efficiency decreased and bias away from the null increased as the true exposure-response parameter increased and the skewness of the exposure distribution of the risk-sets increased. This became more pronounced when the number of cases in the cohort was small. Conclusions: Gains in relative efficiency and bias reduction can be realized by sampling more than the 5-10 controls per case generally recommended, especially when there are few cases, a strong exposure-response relation and a skewed exposure variable.

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BIAS ASSOCIATED WITH SYSTEMATIC ERROR IN A BINARY DEPENDENT REGRESSION VARIABLE. *Gary Fraser, Michael Orlich (Loma Linda University, Loma Linda CA 92350)

When disease endpoint data are ascertained by questionnaire for instance, it is likely that the positive and negative predictive values(PPV, NPV) will deviate from 1.0, often substantially. Moreover, it is possible that these errors may depend in part on the exposure of interest. We restrict attention to a binary exposure, for simplicity. For instance, the accuracy of self-report diagnoses will probably depend on interactions with the medical care system, may in turn depend on education, BMI, dietary patterns etc., factors which could also be the exposures of interest. Even if PPV and NPV do not depend on the exposure, where they are less than 1.0, in general this will still cause bias. An equation and examples describing this will be presented. Let D refer to true disease assignment, d to self-report; P is true prevalence, OR is odds ratio, j = 0, 1 refers to the two levels of the exposure variable, and RB_β(relative bias of logistic β) = $(\beta_d-\beta_D)/\beta_D$. An example illustrating the results of such errors is where $P_0 = 0.02$; $P_1 = 0.03$; so $OR_D = 1.515$; Let NPV = 0.99; PPV = 0.80, both equal for j = 0,1. Then $OR_d/OR_D = 1.337$, and $RB_\beta = 0.711$, a serious bias. Metrics (θ_j,δ_j) different from PPV and NPV, that describe false positive and false negative errors, result in a simple equation to describe bias, and also easily identify rare situations where such errors cancel each other. This equation is $OR_d/OR_D = (\delta_1.\theta_0)/(\delta_0.\theta_1)$, where θ and δ refer respectively to the relative distances that PPV (NPV) are through the range of their possible values. This assumes that PPV > P, and NPV > 1-P i.e. the self-report carries some information about D. Figures will illustrate the effects of such errors in dependent variables to cause bias. We conclude that, in the absence of a corrective procedure, perhaps based on a calibration sub-study, regression analyses where there are more than trivial proportions of false positives or negatives, will often be seriously biased.

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RESPONSE RATE AND TIME TO RESPONSE FOR PATIENT REPORTED OUTCOMES COLLECTED USING A CENTRALIZED SYSTEM IN TWO AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK CANCER SCREENING TRIALS. *Ilana Gareen, Fenghei Duan, Brad Snyder, JoRean Sicks (Brown University, Providence RI 02912)

Patient Reported Outcomes (PRO) are increasingly recognized as clinically important endpoints. We used a central Outcomes and Economics Assessment Unit (OEAU) to administer questionnaires at time points that did not correspond with a clinic visit for two American College of Radiology Imaging Network (ACRIN) screening trials: the National Lung Screening Trial (NLST) and the National CT Colonography Trial (NCTCT). The NLST questionnaire was mailed at 1 month post-screen and included standardized quality of life tools. The NCTCT questionnaire was mailed at 2 weeks post-screen and collected data on procedure preference and intent to return for future screens. In both studies, questionnaire return was requested within 30 days of mailing. Questionnaires were accepted until 180 days of mailing. OEAU staff monitored participant responses and encouraged form completion. We assessed factors associated with questionnaire return using a log multinomial model (return < 30 days, 30-180 days, or not returned). 90% of the NLST questionnaires and 87% of NCTCT questionnaires were returned to the OEAU within 180 days. In NLST, late response was positively associated with increasing age for black women: Risk Ratio[RR] (5 year increase) = 1.79 (95% confidence interval [CI]: 1.36,2.36), but was inversely associated with late response for white men: RR (5 year increase) = 0.73 (95% CI:0.65,0.83). In the NCTCT, which recruited a younger population, late response was inversely associated with younger age, RR(5 year increase) = 0.90 [95% CI: 0.83, 0.98]. We demonstrated that PROs can be effectively collected from a central site in multi-center trials and identified factors associated with late and non-response. In future studies, we can focus additional efforts on populations less likely to return questionnaires in a timely fashion. This study was supported by the National Cancer Institute through the grants U01 CA079778 and U01 CA080098.

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INFLUENCE OF CYP2A6 *4 GENOTYPES ON SERUM COTININE AMONG NON-SMOKING CHINESE PREGNANT WOMEN: IMPLICATION FOR SECONDHAND SMOKE MEASUREMENT. *Chuanbo Xie, Xiaozhong Wen, Peng Ding, Tao Liu, Yanhui He, Zhongzheng Niu, Xiaoying Wu, Shanyu Zhou, Jianmiao Lin, Xiaoling Guo, Weiqing Chen (Department of Biostatistics and Epidemiology, School of Public Health, Sun Yat-Sen University, Guangzhou Guangdong China)

Objective: To investigate the influence of CYP2A6*4 genotypes on serum cotinine among non-smoking pregnant women and assessed its implication for measuring secondhand smoke (SHS) exposure during pregnancy. Methods: We analyzed 545 Chinese non-smoking pregnant women enrolled in a case-control study on SHS and birth outcomes in Guangdong, Southern China. Participants self-reported their SHS exposure status and duration during pregnancy in hospital for delivery. PCR was used for CYP2A6*4 genotyping, and ELISA for measuring serum cotinine. We stratified women by their self-reported SHS exposure status and CYP2A6*4 genotypes, and then compared their median concentration of serum cotinine among women with Kruskal-Wallis and Nemenyi tests. Results: In our sample, 16.3% of pregnant women had CYP2A6*4 allele; and the genotype frequencies of CYP2A6*1/*1, CYP2A6*1/*4 and CYP2A6*4/*4 were 69.7%, 27.9% and 2.4%, respectively. Pregnant women who self-reported SHS exposure have higher median serum cotinine (3.06 ng/ml) than those who self-reported non-SHS exposure (2.27 ng/ml). Among women who self-reported non-SHS exposure, the median cotinine levels were 2.83, 1.39 and 0.77 ng/ml for those with CYP2A6*1/*1, CYP2A6*1/*4 and CYP2A6*4/*4 genotype, respectively. Among women who self-reported SHS exposure, the median cotinine levels were 3.32, 2.37 and 1.56 ng/ml for those with CYP2A6*1/*1, CYP2A6*1/*4 and CYP2A6*4/*4 genotype, respectively. Strikingly, self-reported SHS exposed women with CYP2A6*1/*4 or CYP2A6*4/*4 genotype had significantly lower (rather than higher) median cotinine level than self-reported non-SHS exposed women with CYP2A6*1/*1 (P-value, 0.012). Conclusion: In our sample, CYP2A6*4 genotype was associated with lower serum cotinine among non-smoking pregnant women. Measuring CYP2A6*4 genotype may help to improve the validity of SHS measure by serum cotinine among pregnancy women.

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TEEN PREGNANCY IN THE UNITED STATES IS HIGHER WHEN THE NATIVITY OF THE MOTHER IS INSIDE THE US. *Jagjit Singh Teji, Gurlal S Brar, Ramanpreet K Brar (University of Chicago, Oak Brook IL 60523)

Background: As the latest vital statistics have shown that teen pregnancy is dropping in the US while there are sporadic studies implicating that teen pregnancy in the US is less likely when the nativity of the mother is outside the 50 states of the US. Purpose: To test the hypothesis that teen pregnancy is lower in the mothers whose nativity is outside the 50 states of the US. Methods: VSS data from the NCHS was analyzed for the years 1995 thru 2002. Logistic regression analysis was performed with the dependent variable teen pregnancy, TP, with maternal place of birth, MPB as independent variable. The confounding variables were maternal race, gestational age, GA, birth weight, BWT, maternal conditions such as diabetes, hypertension, pregnancy induced hypertension, maternal exposure to alcohol and tobacco. Also considered variables were prenatal care, plurality, and gender. Stata 12.0 was utilized for statistical analysis. Results: Out of over 31 million records for births during the period 1995 thru 2002 over 25 million births had usable data. Over all, births to teen mothers were significantly more likely if their nativity was within the 50 states of the US, OR 2.49 cf (95%) 2.48-2.50 while controlling for other confounders. Every ethnicity and race was affected by the maternal nativity. Conclusion: 1. We accept the hypothesis that teen pregnancy is lower when the maternal nativity is outside the US. 2. Reason for higher teen pregnancy rates when mother's nativity is from the US is concerning and needs to be decreased.

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GENERAL AND ABDOMINAL OVERWEIGHT/OBESITY INCREASES THE RISK OF PHYSICIAN-DIAGNOSED ASTHMA IN NORWEGIAN ADOLESCENTS: THE YOUNG-HUNT STUDY. *Kathryn B Egan, Adrienne S Ettinger, Turid Lingaas Holmen, Michael B Bracken (Yale Center for Perinatal, Pediatric and Environmental Epidemiology, New Haven CT 06510)

Background: The associations between childhood physician-diagnosed asthma and overweight/obesity are not conclusive. We examined the association between asthma and overweight/obesity, defined by age- and sex-specific body mass index (BMI) and high waist circumference (WC), in two cohorts of adolescents (Young-HUNT (YH)) enrolled in the Nord-Trøndelag Health Study in 1995-1997 (YH1, N = 8,222) and 2006-2008 YH3, N = 7,403) in Trondheim, Norway. Method: Subjects aged 12-19 years completed a health questionnaire in school. Weight, height, and WC were measured. Asthma was defined by self-reported physician-diagnosis of asthma. General overweight was defined by the international age- and sex-specific BMI cutoffs. Abdominal overweight and obesity, respectively, were defined by WC $\geq$ 85th and <95th% and WC $\geq$ 95th % for age and sex. Multiple logistic regression, controlling for overall health, allergic conditions, bronchitis, smoking, chronic illness, socioeconomic factors, doctor and hospital visits, was used to calculate adjusted odds ratios (OR). Results: Physician-diagnosed asthma was reported by 11.8% and 17.0% of adolescents in YH1 and YH3, respectively. Age- and sex-specific general overweight ($\geq$85th% BMI) was associated with a 31% (OR 1.31, 95% CI: 1.06, 1.62) and a 50% (OR 1.50, 95% CI: 1.25, 1.80) increased odds of asthma in YH1 and YH3, respectively. Abdominal overweight was associated with a 28% increased odds (OR 1.28, 95% CI: 1.09, 1.52) in YH3, despite no association in YH1. General plus abdominal overweight ($\geq$85th% WC) was associated with a 43% (OR 1.43, 95% CI: 1.14, 1.78) and a 51% (OR 1.51; 95% CI: 1.26, 1.81) increased odds of asthma, respectively, in YH1 and YH3. Associations stratified by sex were consistent with overall associations. Conclusions: Both general and abdominally overweight/obese adolescents are at increased odds of physician-diagnosed asthma in comparison to normal weight children and this does not vary by sex and increased over time.

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MARKER OF BONE FORMATION AND ORAL INFLAMMATION IN CHILDREN. *Khady Ka, Belinda Nicolau, Mélanie Henderson, Simon Tran, Mari Kaartinen, Vamsee Dhar Myneni, Marie-Claude Rousseau (Oral health and Society Unit, Faculty of Dentistry, McGill University, Montreal QC Canada)

Background: Bone remodeling regulates energy metabolism and glucose homeostasis through the action of osteocalcin, a hormone secreted by osteoblasts during bone formation. Both obesity and diabetes are associated with periodontal diseases. Although a negative association between osteocalcin and adult periodontal diseases has been shown, no studies have investigated this association in children. Moreover, most of the adult studies used total osteocalcin, which includes both carboxylated and uncarboxylated forms, when the latter is suggested to be the active form of the hormone. Aim: To examine the extent to which serum uncarboxylated osteocalcin (ucOC) was associated with a marker of oral inflammation, gingival crevicular fluid tumor necrosis factor alpha (GCF-TNF-α), in Caucasian children. Methods: We used data from the QUebec Adipose and Lifestyle InvesTigation in Youth cohort, an ongoing longitudinal study investigating the natural history of obesity among Caucasian children in Quebec, Canada. This cross-sectional analysis from the baseline visit includes 120 children aged 8–10 years, for whom data was available for both total serum ucOC and TNF-α. Serum ucOC and GCF-TNF-α level were both determined by enzyme-linked immunosorbent assay. Descriptive statistics and linear regression analyses adjusting for potential confounders (age, sex, family income, dental plaque severity, Tanner developmental stage, daily physical activity, and fasting glucose) were conducted, with TNF-α level as the dependent variable. Results: Mean serum ucOC and GCF-TNF- α levels were 19.13 ng/ml and 416.33 pg/ml respectively. A 1-ng/ml increase in serum ucOC was associated with a 0.8% decrease (95% confidence interval: -1.58, -0.09) in GCF-TNF-α level. Conclusion: A negative association between serum ucOC and GCF-TNF-α level was observed. Our findings suggest a complex and dynamic interaction between bone metabolism, energy/glucose homeostasis and oral inflammation.

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CHANGES IN RATES OF PHARMACOTHERAPY FOR CHILDREN WITH FAMILIAL HYPERCHOLESTEROLEMIA BETWEEN 2004 AND 2010. *Nina Joyce, Gregory Wellenius, David Dore, Justin Zachariah (Brown University, Providence RI 02903)

Background: Familial hypercholesterolemia (FH) is a genetic condition characterized by congenital elevation of low density lipoprotein cholesterol levels. FH increases the risk of early atherosclerosis by 20 to 100 fold. Treatment for FH is available in the form of lipid lowering therapy (LLT). In 2008, the American Academy of Pediatrics recommended pharmacotherapy for children as young as 8. However, to date, there has been no assessment of the rate of LLT therapy in the FH population. Methods: We estimated the overall rate of LLT treatment in a commercially insured population of children between the ages of 2 and 20 with an ICD-9 diagnosis of FH. We used a log binomial regression to estimate the unadjusted risk of LLT treatment over time, regressing a linear time trend on the presence or absence of LLT treatment. We tested for effect modification of the time trend by including an interaction term between time and obesity, hypertension/high BP and diabetes. Result: Between 2004 and 2010 we identified 118,515 children with physician diagnosis of FH. Of these 3,180 (2.68%) were treated with an LLT. Between 2004 and 2010 the annual incidence of LLT treatment decreased from 1.3% (601) to 0.28% (143) of untreated children with FH, with an annual mean decrease of 15% (RR 0.85, 95% CI 0.83–0.86, $p < 0.001$). The rate of decline was larger among children with diabetes (RR 0.93, 95% CI 0.83-0.87, $p < 0.05$), although there was no significant difference among children with hypertension or obesity. Conclusion: Despite recommendations that children with FH be treated with LLT, rates of treatment are low and have been declining. The presence of lifestyle related comorbidities did not increase the likelihood for LLT as some feared, and in fact rates decreased among children with diabetes. Future work will address the treatment gap in children with FH and will have relevance on claims that lifestyle cardiometabolic conditions are being inappropriately treated.

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THE PREVALENCE OF HYPOSPADIAS IN DENMARK.

*Jan Wohlfahrt, Tine H Schnack, Nete Munk Nielsen, Charlotte Myrup, Mads Melbye (Department of Epidemiology Research, Statens Serum Institute, Copenhagen Denmark)

Purpose: To analyse the register based prevalence of hypospadias in Denmark taking non-causative factors such as alterations in registration practices and recommendations for treatment of hypospadias into account. Materials and Methods: Based on information from the Danish Hospital Discharge Register we identified 5167 Danish born males with a diagnosis of hypospadias (1980-2007). We calculated the annual cumulative risk (CR) of being registered with a diagnosis or a surgery code for hypospadias before the age of one month and one, six and 20 years of age, respectively. Result: When considering all hospital contacts for males < 20 years there appeared to be an increase in the annual CR of hypospadias during 1980-2007. CR for inpatients only, 1980-2001 however, seemed to be stable, but a steep increase in the age group 1-6 years during 2002-2003 was still present. Furthermore we found an increased CR of having confirmatory surgery in the period 1990-2007, again most pronounced 2002-2003. Interestingly the proportion of inpatients that also had surgery performed increased from 35% to 67% in the period 1980 to 2007. Conclusion: The CR of being diagnosed with hypospadias in Denmark did not changed during 1980-2001. However, a steep increase was observed during 2002-2003 in the age group one to six years. This increase is most likely caused by changes in registration and surgical activity. Thus we found no convincing evidence for an increase in the occurrence of hypospadias in Denmark.

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DOES INFORMAL CHILD CARE AFFECT ADOLESCENT PSYCHOSOCIAL HEALTH? EVIDENCE FROM HONG KONG'S "CHILDREN OF 1997" BIRTH COHORT.

*Cherry Y Leung, Tai Hing Lam, Gabriel M Leung, Shi Lin Lin, C Mary Schooling (School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR China)

In Western populations, informal child care is often associated with negative short-term cognitive outcomes while parental care may be important in promoting child social adjustment. In non-western settings, it is relatively common for sustained informal child care to be provided by family members, such as grandparents, or by a family employee at home. Concern exists as to how such arrangements affect child development. The authors examined the association of child care (parents, grandparents and family employee) at 6 months, 3 years, 5 years, and 11 years with child behavior, self-esteem, and depression in early adolescence in a setting where formal child care (day care) is rare. Multivariable linear regression was used in the "Children of 1997" Chinese birth cohort to examine the associations of child care with parent-reported Rutter score for child behavior at ~11 years (n = 5598, 68% response rate), self-reported Culture-Free Self-Esteem Inventory score at ~11 years (n = 7112, 86% response rate) and self-reported PHQ-9 depressive symptom score at ~14 years (n = 5797, 70% response rate). Analyses adjusted for sex, mother's place of birth, highest parental education, household income and maternal age at birth. Multiple imputation was used for missing exposures and potential confounders. Informal child care at any age by grandparents or family employee was unrelated to child behavior, self-esteem or depressive symptoms, including 6 months which is a crucial age for child development [grandparents for behavior -0.08, 95% confidence interval (CI) -0.62 to 0.46, self-esteem -0.21, CI -0.90 to 0.49, and depressive symptoms 0.07, CI -0.22 to 0.37; family employee for behavior 0.21, CI -0.43 to 0.85, self-esteem -0.53, CI -1.23 to 0.16, and depressive symptoms, CI 0.27, -0.04 to 0.57]. In a non-western context informal child care does not appear to affect adolescent psychosocial health.

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PERCEIVED WEIGHT, NOT BODY MASS INDEX: A STRONG PREDICTOR OF SUICIDE RISK AMONG US ADOLESCENTS.

*Dana Mowls, Melissa Zullo, Vinay Cheruvu (Department of Epidemiology and Biostatistics, College of Public Health, Kent State University, Kent OH 44242)

Adolescent perception of weight may have a greater effect on suicide risk than body mass index (BMI). The purpose of this research was to examine the association between BMI and suicide risk and to determine if perceived weight mediates the relationship. Cross-sectional data were from the 2009/2011 Youth Risk Behavior System (n = 23,008). Suicide risk was based on four questions: (i) feelings of sadness (ii) suicide ideation (iii) suicide plan, and (iv) suicide attempt. Low-risk included (i) with or without (ii) and high-risk included (i) (ii) (iii) with or without (iv). Multinomial logistic regression models examined the association between BMI and suicide risk and determined mediation adjusting for all confounders. BMI was significantly associated with low-risk ($p = 0.03$) and marginally associated with high-risk ($p = 0.09$) for suicide in overweight or obese adolescents without perceived weight in the model. When perceived weight was added to the model, the association between BMI and suicide risk became non-significant, suggesting perceived weight completely mediates the relationship. Adolescents whose perceived weight was slightly/very underweight or slightly/ very overweight were equally more likely to be at high risk for suicide: [Odds Ratio (OR): 1.8, 95% Confidence Interval (CI): 1.5–2.2]; [OR: 1.8, CI: 1.5–2.1], when compared to adolescents whose perceived weight was normal. In stratified analysis, females whose perceived weight was slightly/very underweight were more likely to be at high risk for suicide [OR: 2.1, CI: 1.6–2.8] followed by their counterpart males [OR: 1.5, CI: 1.1–2.0], when compared to males and females whose perceived weight was normal. Perceived weight, not BMI, is an important predictor of suicide risk among adolescents. These results provide evidence that perceived weight completely mediates the association between BMI and suicide risk, suggesting that body image and self-confidence may play a vital role in suicide risk.

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AGE AT AUTISM SPECTRUM DISORDER (ASD) DIAGNOSIS BY RACE/ETHNICITY AMONG CHILDREN WITH SPECIAL HEALTH CARE NEEDS, 2009-2010 NATIONAL SURVEY OF CHILDREN WITH SPECIAL HEALTH CARE NEEDS (NS-CSHCN).

*Heejoo Jo, Laura Schieve, Catherine Rice, Marshalyn Yeargin-Allsopp, Lin Hui Tian, Stephen Blumberg, Michael Kogan, Coleen Boyle (Centers for Disease Control and Prevention, Atlanta, GA)

The prevalence of diagnosed ASD has increased and mean age at ASD diagnosis age has decreased among US children. Study by race/ethnicity is limited. From the 2009-2010 NS-CSHCN, we selected 3,025 3-17-year-old children whose parent reported a current ASD diagnosis. We compared ASD prevalence and mean and percentage distribution of age at diagnosis across 4 racial/ethnic and primary household language groups: non-Hispanic white, any language (NHWA); non-Hispanic black, any language (NHBA); Hispanic, any race, English (HAE); and Hispanic, any race, other language (HAO). Among children aged >5 years, we additionally assessed findings by ASD severity and adjusted for family sociodemographics. ASD prevalence estimates were 15.3 (NHWA), 10.4 (NHBA), 14.1 (HAE), and 5.2 (HAO) per 1000 US children. Among children aged 3-4 years, mean diagnosis age was comparable across racial/ethnic groups. Among older children, mean diagnosis age was 5.1 (NHWA), 4.6 (NHBA), 4.7 (HAE), and 3.3 (HAO) years. However, while among mild/moderate ASD cases, NHWA children had a significantly higher proportion (53.8%) of late diagnosis (>5 years of age) than NHBA (38.0%) or HAO children (20.3%). Among severe ASD cases, NHWA children had a lower (albeit non-significant) proportion (19.0%) of late diagnoses than NHBA (40.0%), HAE (32.5%), and HAO (34.5%) children. NHWA children have both higher ASD prevalence and a higher proportion of late diagnoses than NHBA and HAO children. The diagnosis age finding is limited to mild/moderate cases. Lower ASD prevalence in these minority groups may reflect failure to identify mild/moderate cases among older children.

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PRENATAL FAST FOOD CONSUMPTION INCREASES THE RISK FOR THE DEVELOPMENT OF ASTHMA IN CHILDHOOD. *Ondine S von Ehrenstein, Marie Flores, Hilary Aralis, Beate Ritz (University of California, Los Angeles CA 90095)

Asthma in children is a global problem, affecting 16% of girls and 21% of boys in North America (International Study of Asthma and Allergies in Childhood, ISAAC). Yet, knowledge about risk factors for the development of child asthma is limited. No study to date has reported on prenatal fast food (FF) intake in relation to child asthma. We investigated whether consumption of FF during pregnancy increases the risk for asthma in children. From 58,316 birth records for children born in 2003 to mothers residing in 111 Los Angeles County zip codes, we selected cases of low weight (<2500g) and preterm birth (PTB) (<37 weeks) and an equal number of randomly sampled controls (≥2,500g/term). We conducted a survey 3-6 months after birth with 2543 of the 6374 women originally sampled from the cohort asking about frequency of FF consumption, demographic and pregnancy-related variables. Of 2438 women who participated in the survey and agreed to being recontacted, 1201 were located and participated in a follow-up in 2006; child asthma/wheeze were assessed using ISAAC asthma questions. Poisson regression models with robust error variance using a log link function were used to estimate relative risks (RR). Maternal consumption of FF during pregnancy increased risks for child wheeze in a dose dependent manner: "once a month": RR: 1.09 (95% CI: 0.71, 1.68), "once a week": 1.38 (0.93, 2.6); "3-4 days a week": 1.84 (1.21, 2.79); "every day" 2.33 (1.40, 3.87) compared to "never", adjusting for potential confounders, including maternal asthma, race/ethnicity, PTB, and measured PM2.5 and ozone during pregnancy. Corresponding estimates for doctor's diagnosed asthma similarly increased (0.99 (0.46, 2.11); 1.15 (0.57, 2.34); 1.80 (0.85, 3.78); 3.22 (1.29, 8.01)) with increasing maternal FF intake. Our findings of increased child asthma risks following frequent FF consumption in pregnancy indicates a frequent and preventable risk factor, and calls for further investigation.

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DIFFERENTIATING INFECTIOUS FROM ISCHEMIC CAUSES OF NECROTIZING ENTEROCOLITIS AMONG PREMATURE INFANTS. *Anayeli Herrera Morales, Aaron Wendelboe (University of Oklahoma Health Sciences Center, Oklahoma City OK 73104)

Introduction: Necrotizing enterocolitis (NEC) is a complex, multifactorial, and poorly understood disease of the gastrointestinal tract occurring chiefly among premature infants. NEC pathogenesis has ischemic and infectious pathways; yet NEC has been studied as a single outcome. There is ambiguity regarding the strength of certain risk factors for NEC; the cause of which may stem from failure to stratify NEC cases according to pathogenic pathway. We aim to understand differences between infectious and ischemic NEC cases for future efforts to create novel predictive risk models according to the cases' etiologic pathway. Methods: We conducted a case-control study of premature infants with NEC at a neonatal intensive care unit in Oklahoma. Case infants were ≤36 weeks gestational age diagnosed with NEC according to modified Bell's criteria. A directed acyclic graph was developed to differentiate between infectious and ischemic cases and better understand relationships between potential risk factors. We used t-tests and chi-square tests to detect differences, and computed odds ratios (OR) with 95% confidence intervals (CI). Results During 2005 to 2009, 54 cases were enrolled. Twenty four (44.4%) cases were classified as infectious NEC while 30 (55.6%) were ischemic NEC. Among all cases, infectious cases had significantly lower birth weight (bw) and younger gestational age (ga) than ischemic cases (meanbw = 1000 g vs. 1265 g, $p < 0.001$; meanga = 189 days vs. 205 days, $p < 0.001$). Males had 2.3 higher odds of being an infectious case vs. being an ischemic case (95% CI: 1.1-4.6). The distribution of race was not significantly different ($p = 0.16$). Conclusion As infectious cases of NEC are significantly younger and have lower birth weights than ischemic cases, analyzing risk factors for NEC may differ by etiologic pathway as well. The relationship between males and infectious NEC needs additional investigation.

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DO PRESCHOOL WHEEZE PHENOTYPES PREDICT ALLERGIC DISEASE OUTCOMES IN ADOLESCENCE?15 YEAR FOLLOW-UP OF THE CANADIAN CHILDHOOD ASTHMA PRIMARY PREVENTION STUDY. *Meghan B Azad, Anita L Kozyrskyj, Edmond S Chan, Moira Chan-Yeung, Allan B Becker (University of Alberta, Winnipeg MB Canada)

RATIONALE: There is increasing evidence that different patterns of wheezing during childhood may be associated with different long term prognoses. In a high-risk birth cohort, we aimed to describe the distribution of preschool wheeze phenotypes and their association with allergic disease outcomes in adolescence. Methods: The study included 459 subjects from the Canadian Childhood Asthma Primary Prevention Study. Preschool wheeze phenotypes, as defined in the Tucson birth cohort (NEJM 1995 332:133-38), were assigned based on parent-reported wheeze at six time points from birth to age 7. At age 15, 326 subjects were evaluated for the following allergic disease outcomes: wheeze (self report), lung function (spirometry), atopy (skin prick testing), and clinical diagnosis of asthma and food allergy. Associations were assessed by logistic regression with adjustment for gender, city and study group. Results: The overall distribution of preschool wheeze phenotypes was: 51% never wheezers, 28% transient early wheezers, 8% late-onset wheezers, and 13% persistent wheezers. The phenotype distribution was significantly different between genders ($p = 0.04$) and between cities ($p < 0.01$), but not between study groups. By age 15, the risk of asthma was significantly increased among all "wheezing" phenotype groups compared to never wheezers, and was highest among persistent wheezers (adjusted odds ratio and 95% confidence interval; 13.9, 5.3-36.6). The risks of current wheeze, airway hyper-responsiveness, atopy and food allergy were all elevated among late-onset wheezers and persistent wheezers, but not among transient early wheezers. Conclusion: Patterns of wheezing during the preschool years are associated with allergic disease outcomes in adolescence. Late-onset and persistent wheezers are at increased risk for allergic disease, especially asthma. Transient early wheeze also elevates risk for asthma, but imparts no additional risk for atopy or food allergy.

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DISPARITIES OF BREASTFEEDING PATTERNS BETWEEN BLACK AND WHITE WOMEN IN NORTH AMERICA. RESULTS FROM THE AHS-2. *Sozina Katuli, Keiji Oda, Raymond Knutsen, Synnøve Knutsen (Department of Epidemiology, Biostatistics and Population Medicine, Loma Linda CA 92354)

Background: Racial disparities of breast feeding have been reported in various studies, but few have evaluated the factors associated with racial discrepancies in breastfeeding. Method: We evaluated breastfeeding patterns among 24,436 white and 10,196 black parous females, aged 30-80 years, who were enrolled in the Adventist Health Study-2, a cohort of 96,000 health conscious subject across the US and Canada. Two outcomes were evaluated: 1) initiation of breastfeeding and 2) length (months/child) of breastfeeding using multiple logistic and multiple linear regression, respectively. Analyses were adjusted for age, education, parity, body mass index, marital status, country lived during young adult life (age 16-25), oral contraceptive use and dietary patterns. Results: Black women were less likely to have breastfed than white women (Odds Ratio = 0.37, 95% Confidence Interval: 0.34-0.41) and breastfed on average 1.2 months shorter per child than white women. Older women were less likely to have breastfed their children (OR = 0.77, 0.41, 0.30 for ages 41-50, 51-60 and 61-80 respectively compared to 30-40 year olds (p-trend <0.001). Vegetarians were more likely to initiate breast feeding than non-vegetarians (OR = 2.01). Other independent predictors of initiation of/duration of breastfeeding were age, education, living outside of the US at age 16-25, parity, marital status,BMI and oral contraceptive use. Conclusions: Black women were less likely to initiate breastfeeding and, if breastfeeding, did so for fewer months than white women. The racial difference remained virtually unchanged even after adjusting for a number of socio-economic factors including age, marital status, education and place lived during early adulthood. The observed racial disparity warrants further study into possible factors that can explain the strong differences seen. Attitudes towards breastfeeding, in particular, need to be investigated among blacks and white females in the US.

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HEALTH OF INDIGENOUS PEOPLES: A GLOBAL HEALTH DISPARITY. *Ezra Susser (Columbia University, New York NY 10032)

Indigenous peoples tend to have poorer health status than other populations within the same country. This inequality pertains to low, middle, and high income countries, as well as to countries in different regions of the globe. Thus, despite the great diversity of indigenous peoples, this inequality represents a global health disparity and merits high priority in epidemiologic research. The three speakers in this symposium are experts on the health of indigenous peoples in three regions of the globe. Two have ancestral roots in these indigenous groups. Carlos Coimbra Jr will focus on health and nutrition among indigenous children in Brazil, presenting results from the first national indigenous health survey as well as other studies he has conducted. Sandra Eades will present data on the health, social and economic conditions of Australia's Aboriginal people and describe an ongoing mutigenerational study of Aboriginal health. Sally H Smith will discuss the health of indigenous peoples in Alaska; and will place these findings within a broader perspective that encompasses Arctic peoples spread over 8 countries in the circumpolar region. The presentations will show how each indigenous group presents very different challenges for epidemiology, public health, and reduction of social inequalities. At the same time, they will reveal commonalities, such as the ongoing impact of historic discrimination and the impact of current socioeconomic and epidemiologic transitions on the lives and culture of these peoples. As discussant, Patricia Buffler will draw out both commonalities and differences, and highlight the implications for global epidemiology and public health.

Speakers:

1. Carlos E.A. Coimbra, Jr., Fundação Oswaldo Cruz, Rio de Janeiro
2. Professor Sandra Eades, Sydney School of Public Health., The University of Sydney
3. Sally H. Smith, Board of Directors, Alaska Native Tribal Health Consortium.

Discussant: Patricia Buffler, President-elect, International Epidemiology Association. Professor of Epidemiology, School of Public Health, University of California Berkeley

[Sponsored by the International Epidemiology Association]

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MOVING FROM WHY TO HOW: DEALING WITH THE PRACTICAL CHALLENGES OF ADOPTING SYSTEMS SCIENCE APPROACHES IN EPIDEMIOLOGY. *Abdulrahman El-Sayed (Columbia University, New York NY 10032)

The past 10 years have a seen a growth in interest in systems approaches in epidemiology. A fair body of literature in the field has discussed how these methods, in theory, can capture non-linearity, dynamic feedback loops, and emergence in policy-relevant epidemiologic research. However, while calls for these approaches have grown, empiric analyses that have effectively used these approaches to yield new insight regarding the etiology of high-burden diseases lag behind. Systems epidemiology is hampered by a paucity of guidelines, best practices, and illustrative applications of systems tools to epidemiologic questions. In this symposium, we will move the discussion beyond arguments about why systems approaches can move epidemiology forward, to a discussion about how to do so. By bringing together thought leaders in the field to discuss questions central to systems epidemiology including (a) the scope of questions over which systems tools may have dominion (b) how best to parameterize and validate systems models, and (c) the appropriate interpretation of results from systems models, we aim to educate epidemiologists beginning to use these tools in their own work regarding how best to approach them.

Speakers:

1. *Evaluating agent-based network models for health and behaviors* - David Shoham
2. *Racial/ethnic differences in alcohol-related injury: an agent-based modeling approach* < - Katherine M Keyes
3. *Adapting systems approaches for epidemiology: An illustration considering the social communicability of obesity* - Abdulrahman M El-Sayed

Discussant: Ichiro Kawachi

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STATISTICAL METHODS IN LIFECOURSE EPIDEMIOLOGY. *Kate Tilling (University of Bristol, Bristol United Kingdom)

There is increasing emphasis in epidemiological and medical research about how exposures across the lifecourse interact with one another to influence later health. Answering questions about the relative importance of magnitude and timing of growth, behaviour and health status throughout the lifecourse requires appropriate analyses of longitudinal data and careful specification of hypotheses. Commonly-used methods for analysing repeated measures are too limited to accommodate the complexities of lifecourse analyses. More complex methods, such as multilevel models, latent class analyses and their extensions, are becoming increasingly available and used in relating lifecourse exposures to outcomes. Different hypotheses lead to different model choices, and the extent to which models are suitable for a given question is not always clear. In this symposium we present four examples of lifecourse questions tackled using different statistical approaches: latent class models; multivariate multilevel models; multilevel linear spline models and marginal structural models. The applications presented vary across the lifecourse, from birth to later life. We will discuss the advantages and disadvantages of the approaches used, and highlight the different hypotheses that can be tested by each approach.

Speakers:

1. *Modelling trajectories of growth: A multilevel modelling approach* - Dr. LD Howe, University of Bristol
2. *Marginal structural models for life-course epidemiology: An example of breastfeeding and health consequences in early childhood* - Dr. Rolf H.H. Groenwold, University Medical Center Utrecht
3. *Multivariate multilevel models for asociations between trajectories and outcomes: An example of gestational weight gain and birthweight* - Prof K Tilling, University of Bristol
4. *Modeling trajectories of change in physical activity and all-cause mortality: A latent class approach* - Dr. Qian-Li Xue, Johns Hopkins University

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SURVIVING COMPETING RISKS. *Steve Cole, Brian Lau (University of North Carolina, Chapel Hill NC 27599)

Survival analyses are central to epidemiologic research. In such analyses, the occurrence of an event of interest is often precluded by a competing event/risk. This competing-risk situation occurs frequently in epidemiologic research. However, formal methods (with estimators tailored to account for competing risks) are rarely employed in epidemiologic studies. Furthermore, much confusion exists among epidemiologists about competing risks and analytical methods for data with competing risks. This confusion is due in part to the different frameworks for envisioning competing events (multistate versus latent failure times), and the question of whether an assumption of independence between the event of interest and the competing event is necessary to obtain a consistent estimator. This symposium will: 1) review competing-risk frameworks, 2) illustrate the use of regression models which account for competing risks in epidemiologic data, 3) describe new extensions to regression models for competing risks, and 4) discuss future directions for competing risk methods (e.g. the adverse/benefit ratio).

Speakers:

1. *Competing risks: the risks compete, the hazards add* - Bryan Lau (Epidemiology, JHU)
2. *Estimating risk differences and risk ratios from cohort studies with competing risks* - Steve Cole (Epidemiology, UNC)
3. *Recent developments in competing risks* - Jason Fine (Biostatistics, UNC)

Discussant: James Robins

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WHAT IS THE ROLE OF EPIDEMIOLOGY IN THE ERA OF MOLECULAR BIOLOGY AND GENOMICS. *Lewis Kuller (University of Pittsburgh, Pittsburgh PA 15213)

The relevance of epidemiology as an important research discipline has recently been questioned in papers published in the American Journal of Epidemiology. Critical questions include: 1) whether methodology currently applied in genomic studies that are not hypothesis-driven or requiring well-defined population samples, rather, very large populations with modest data collection, i.e. quantity versus quality, will be the norm for epidemiological studies; 2) whether the advances in molecular biology, including epi-genetic microRNA, microarray analysis of somatic mutations, proteomics, metabolomics, other -omics, will provide a better measure of exposures to lifestyles, such as nutrition, environmental toxins or infectious agents, and obviate or reduce the need for traditional measures of exposures in epidemiology studies; and 3) will the new molecular biology technologies result in reclassification of specific diagnostic categories, especially in cancer. Will these classifications based on molecular biology require a revision of the interpretation of previous epidemiological studies? A new discipline has been proposed that combines epidemiology and molecular biology, molecular pathology epidemiology. Epidemiology is a basic science of public health and preventive medicine, providing estimates of population risk, e.g. the Framingham risk score. Molecular biology and genomics focus on identifying individual-specific risk, e.g. personalized medicine, especially for therapeutic decisions, e.g. gene therapy or aspirin in the treatment of colon cancer. Is the traditional epidemiological risk factor associations antiquated? Will the immediate future include genomic analysis at birth that will determine individual lifetime risk of disease in relationship to specific lifestyle and environmental exposures?

Speakers:

1. *'Deep phenotyping': characterizing populations in the era of genomics and systems biology*. Curr Opin Lipidol 2008;19:151-7 – Russell P. Tracy
2. *Integration of molecular pathology into epidemiology to improve disease phenotyping in population science* - Shuji Ogino
3. *Will methods of quantifying diet improve nutrition, epidemiology research?* – Ross L. Prentice
4. *The challenges for epidemiology of new technologies, large samples, data collection, example of the National Children's Study* – Michael B. Bracken

[Sponsored by the American Journal of Epidemiology]

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THE EFFECT OF RECESSIONS ON SUICIDE MORTALITY IN THE UNITED STATES. *Sam Harper, Thomas Charters, Erin C Strumpf, Arijit Nandi (McGill University, Montreal QC Canada)

Prior work suggests economic downturns are associated with suicide mortality. We estimated the effect of US state economic conditions on rates of suicide mortality for the period up to and including the recent Great Recession, as well as whether the effect differed for population subgroups. Monthly economic conditions for each state were measured by the Index of Coincident Economic Indicators (ICEI), a composite of four indicators of economic activity. Monthly state-specific rates of suicide were calculated using counts of suicide deaths between 1980-2010 from the US vital statistics and population counts from the Current Population Survey. We used negative binomial regression models, controlling for demographics, seasonality, state fixed effects, and state-specific temporal trends, to estimate the effect of changes in the ICEI on the rate of suicide mortality. A 10-unit decrease in the ICEI (similar to that of the Great Recession) was associated with an incidence rate difference (RD) of 0.134 [95% confidence interval [CI]:0.015,0.253] suicides per 100,000 population. The effect was stronger among men (RD = 0.190, 95% CI: 0.042,0.339) than among women (RD = 0.048, 95% CI:-0.282, 0.379). The effects of economic downturns were most pronounced among those with the least educational attainment: a 10-unit decrease in the ICEI was associated with rate differences of 0.419 (95% CI:0.106, 0.732), 0.174 (95% CI:-0.117, 0.466), and 0.010 (95% CI:-0.109, 0.216) among those with less than a high school education, high school degree, or more than a high school education, respectively. We examined the relation between economic conditions and suicide mortality, building on prior work by including a novel measure of economic conditions and examining whether effects varied across population subgroups. We corroborated findings of countercyclical fluctuations in suicide and showed the effects of downturns were concentrated among the less educated.

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WAR- AND CIVILIAN-TRAUMA EXPERIENCES AND THEIR RELATION WITH SUICIDAL IDEATION AMONG OHIO ARMY NATIONAL GUARD SOLDIERS. *Marta Prescott, Marijo Tamburrino, Joseph Calabrese, Israel Liberzon, Renee Slembarski, Edwin Shirley, Thomas Fine, Toyomi Goto, Philip Chan, James Sizemore, Jeremy Kauffman, Hal Morgenstern, Sandro Galea (Mailman School of Public Health, New York NY 10032)

There is evidence that the experience of trauma is linked to greater suicide risk. Recent studies suggest, however, that the magnitude of this link depends on the type of trauma experienced. Given the alarming increase in suicide rates in the military, we aimed to determine the relation between war- vs. civilian-related traumatic events and suicidal ideation within a military sample. Using a cross-sectional sample of 898 soldiers from the Ohio Army National Guard, we assessed soldiers' experience of war- and civilian- related traumatic events and the presence of suicidal ideation (assessed with the Patient Health Questionnaire-9). Logistic regression was used to estimate the association between trauma type (war vs. civilian) and suicidal ideation among soldiers who had experienced a traumatic event, by posttraumatic stress disorder (PTSD) status (assessed with the PTSD Checklist-17), and adjusting for potential confounders including demographics, traumatic event history, history of psychopathology, and characteristics of the event in question. The proportion reporting suicidal ideation was 9.9% in the total sample. Among the 833 soldiers without PTSD, those who experienced civilian traumatic events were more likely to report suicidal ideation than were soldiers who experienced war-related events (unadjusted odds ratio [OR] = 1.4; 95% confidence interval [CI]: 0.7, 1.5), adjusted OR = 2.4; 95% CI: 1.1, 5.5). A similar association was observed among the 65 soldiers with PTSD (unadjusted OR = 2.6; 95% CI: 0.8, 8.5). Thus, regardless of PTSD status, soldiers who experienced a traumatic event in their civilian lives were more likely to report suicidal ideation than were soldiers who experienced war-related traumatic events. Soldiers' full traumatic event history—including events that may have occurred outside of the military—may contribute to the mental health of returning veterans.

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PHYSICIANS' PRESCRIBING PREFERENCES ARE A POTENTIAL INSTRUMENT FOR PATIENTS' ACTUAL PRESCRIPTIONS OF ANTIDEPRESSANTS. *Neil Davies, David Gunnell, Kyla Thomas, Chris Metcalfe, Frank Windmeijer, Richard Martin, Frank Windmeijer (Medical Research Council Centre for Causal Analysis in Translational Epidemiology, University of Bristol, Bristol Avon UK)

Confounding by indication is a limitation of pharmacoepidemiogical studies using administration data for comparative effectiveness research. Previous studies suggested that physicians' previous prescriptions, a proxy of their prescribing preferences, are valid instruments for their subsequent prescriptions. We investigated whether prior prescriptions are valid instruments for antidepressant prescribing. We used data from the Clinical Practice Research Datalink to investigate whether physicians' previous prescriptions of (a) TCAs vs SSRIs and (b) paroxetine vs. other SSRIs were valid instruments. We tested the validity of the instrumental variable assumptions. Finally we investigated whether suicide or self-harm was more likely in patients prescribed TCAs using both conventional and instrumental variable regression. We identified 897,983 patients prescribed SSRIs or TCAs. Physicians' prior prescriptions were strongly associated with subsequent patients' prescriptions. Physicians who previously prescribed TCAs were 14.9 (95% confidence interval, [CI]:14.4,15.4) percentage points (pp) more likely to prescribe TCAs to their next patient. Physicians who previously prescribed paroxetine were 27.7 (95% CI:26.7,28.8) pp more likely to prescribe paroxetine to subsequent patients. Physicians' previous prescriptions were less associated with patients' baseline characteristics than the patients' actual prescriptions. We found no evidence the instrumental variable results differed from conventional regressions ($p = 0.45$). Physicians' prescribing preferences are valid instruments for evaluating the effects of antidepressants. The main instrumental variable assumptions held: physicians' prior prescriptions were associated with patients' actual prescriptions and less associated with baseline characteristics. However, the instrumental variable results were imprecise and provided little evidence that the conventional results suffered from residual confounding.

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AN OBSERVATIONAL STUDY ON THE IMPACT OF SERVICE USE FOR MENTAL DISORDERS ON SUICIDALITY. *Guilherme Borges, Ricardo Orozco, Mathew Miller, Joshua Breslau (National Institute of Psychiatry Ramon de la Fuente Muniz, Mexico DF Mexico)

Background: Suicide is the tenth cause of death in the US, and treatment of mental disorders is advocated as a mean to lower this rate. Our goal is to report on the association between treatment for mental disorder with the likely reduction in suicide ideation, and on plan and attempts among those with suicide ideation. Methods: Suicidality, service use for mental disorder and mental disorders were assessed using the World Mental Health version of the Composite International Diagnostic Interview. Discrete time survival analysis was used to examine risk for life-time suicidality by the presence of a prior mental disorder and treatment for mental disorder among 15,348 participants in the Collaborative Psychiatric Epidemiological Surveys, a group of cross-sectional surveys. Results: The more suicidality reported the more service use (69% for ideation, 78.6% for a plan and 86.9% for attempt). Any use of service for mental disorders did not preclude the occurrence of posterior suicide ideation if the respondent was free of a mental disorder but was not associated with the further development of an ideation among those with a prior disorder. Among suicide ideators, using any service for mental disorder was associated with a lower likelihood to develop a plan in the expected direction but non-significantly (Odds Ratio (OR) 0.78, 95% CI = 0.55-1.11) while using any service was associated with a lower likelihood of developing an attempt (OR = 0.71, 95% CI = 0.55-0.92), especially among those with a prior mental disorder (OR = 0.62, 95% CI = 0.47-0.83). Conclusions: Treatment among those with a mental disorder did not affect the development of an ideation, may reduce the risk of a plan and was associated with a lower rate of an attempt.

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LIFETIME VIGOROUS PHYSICAL ACTIVITY IN RELATION TO ESTROGEN RECEPTOR-POSITIVE AND ESTROGEN RECEPTOR-NEGATIVE BREAST CANCER IN AFRICAN AMERICAN WOMEN. *Traci N Bethea, Lynn Rosenberg, Julie R Palmer, Kristen L Kipping-Ruane, Lucile L Adams-Campbell (Slone Epidemiology Center at Boston University, Boston MA 02215)

A number of studies have found that physical exercise is inversely related to breast cancer incidence. Whether the association is present for both estrogen receptor positive (ER-positive) and ER-negative breast cancer is uncertain. We assessed the relation of vigorous exercise over the life course to incidence of ER-positive and ER-negative breast cancer in data from the Black Women's Health Study. Participants enrolled in this ongoing follow-up study in 1995 by completing mailed questionnaires; exposure information and cancer incidence data are updated every 2 years. Participants were asked about usual vigorous physical activity in high school, at age 21, at age 30, and at baseline; we used these data to calculate an average lifetime vigorous physical activity variable among women aged 30 and older at baseline who provided data for each time period (N = 44,704). Breast cancer diagnoses were confirmed through pathology reports and cancer registry data. Cox proportional hazard models were used to estimate incidence rate ratios (IRRs) and 95% confidence intervals (CIs) with control for confounding factors. Based on 1,137 invasive breast cancer cases that occurred from 1995 to 2009, average lifetime exercise was not associated with risk of ER-positive breast cancer. For ER-negative breast cancer, the multivariable IRR for an average of 3+ hours/week of vigorous activity was 0.54 (95% CI 0.32-0.92). The strongest associations of vigorous exercise with risk of ER-negative breast cancer were observed among postmenopausal women and among women who had a body mass index of <30, but interactions were not statistically significant. Our results suggest that lifetime vigorous exercise may be associated with a lower risk of ER-negative breast cancer in African American women. This finding is important because ER-negative breast cancer is an aggressive subtype that disproportionately affects African Americans.

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BISPHOSPHONATE USE AND RISK OF POSTMENOPAUSAL BREAST CANCER. *Sarah Aroner, Rulla Tamimi, Bernard Rosner, Susan Hankinson (Harvard School of Public Health, Brookline MA 02445)

Background: Bisphosphonates, a class of widely prescribed osteoporosis drugs, have been associated with a reduced risk of breast cancer in several recent observational studies. However, whether the observed association could be due to confounding by bone mineral density (BMD) is unclear. Low BMD is the main indication for bisphosphonate use and has also been associated with a decreased risk of breast cancer, as BMD is a marker of cumulative estrogen exposure. Methods: We conducted a prospective analysis of bisphosphonate use and breast cancer risk among 62,340 postmenopausal women in the Nurses' Health Study with follow-up from 2002-2010. To investigate whether associations might be confounded by BMD, we examined whether estimates from Cox proportional hazards models changed with adjustment for osteoporosis and other markers of BMD (e.g., body mass index (BMI)) or restriction to women with osteoporosis. To further evaluate whether associations might be due to lower underlying estrogen levels among bisphosphonate users, we compared geometric mean plasma estradiol levels among ever and never bisphosphonate users. Results: During 422,740 person-years of follow-up, 1535 invasive breast cancer cases were observed. In age-adjusted analyses, 5 or more years of bisphosphonate use was associated with lower risk of breast cancer compared with never use (hazard ratio [HR] = 0.81, 95% confidence interval [95% CI]: 0.66, 0.99). In multivariate models, this association was attenuated (HR = 0.91, 95% CI: 0.72, 1.13), with osteoporosis and BMI accounting for most of the attenuation. Associations were also null in analyses restricted to women with osteoporosis. Geometric mean plasma estradiol levels, adjusted for BMI and other covariates, were 5% lower among bisphosphonate users compared with non-users ($p = 0.0007$). Conclusion: Although bisphosphonate use was associated with lower risk of breast cancer, this appeared to be attributable to confounding by BMD.

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FEASIBILITY AND PERFORMANCE OF NCI'S AUTOMATED SELF-ADMINISTERED 24 HOUR RECALL (ASA24). *Frances Thompson, Sujata Dixit-Joshi, Nancy Potischman, Sharon Kirkpatrick, Gwen Alexander, Laura Coleman, Lawrence Kushi, Michelle Groesbeck, Maria Sundaram, Heather Clancy, Deirdre Douglass, Beth Mittl, Stephanie George, Amy Subar (U.S. National Cancer Institute, Rockville MD 20850)

Background: The interviewer-administered 24-hour recall (24HR) is considered one of the better instruments to capture dietary intake, but the method is expensive. The National Cancer Institute (NCI) developed the Automated Self-Administered 24-hour Recall (ASA24) to facilitate the collection of 24HRs in large-scale studies. The Food Reporting Comparison Study (FORCS) assessed the feasibility and quality of data collected using ASA24 compared to the USDA's interviewer-administered Automated Multiple Pass Method (AMPM) recall. Methods: About 1200 men and women ages 20 to 70 years were recruited from three integrated health systems - Marshfield Clinic (WI), Henry Ford Health System (MI), and Kaiser-Permanente Northern California (CA) - using quota sampling to ensure a range of ages and race/ethnicity groups. Participants were asked to complete two 24HRs, 4-7 weeks apart, and were offered financial incentives; they were randomized into four study groups: 1) two ASA24s; 2) two AMPMs; 3) one ASA24 and one AMPM; and 4) one AMPM and one ASA24. Results: 95% (n = 1183) of enrolled participants completed at least one 24HR; 80% completed two. 24HR completion rates were similar across all four study groups. Mean reported intakes on the ASA24 were similar to those on the AMPM for the dietary components examined thus far: energy (2132 vs. 2126 kcal), fat (84.9 vs. 82.8 g), saturated fatty acids (27.9 vs. 26.9 g), fiber (18.4 vs. 18.4 g), and cup equivalents of fruits and vegetables (3.0 vs. 3.1). Conclusion: In this large field study with diverse participants, response rates and mean reported dietary intake between the self-administered online ASA24 and interviewer-administered AMPM were similar. The ability to obtain high quality dietary data using a web-based instrument is significant to epidemiologists.

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VEGETARIAN DIETARY PATTERNS ASSOCIATED WITH BIOMARKERS OF CANCER RISK. *Karen Jaceldo-Siegl, Jing Fan, Ella Haddad, Synnove Knutsen, Denise Bellinger, Gary Fraser (Loma Linda University, Loma Linda CA 92350)

Epidemiologic investigations link various types of cancers with the insulin-like growth factor (IGF) system, biomarkers of inflammation, and body mass index (BMI). Several environmental factors have been identified as having influence on cancer biomarkers. Diet is thought to be important among these factors. We examined the associations of demographic, dietary patterns and other lifestyle factors with circulating levels of insulin, IGF-1, IGFBP-3, C-reactive protein (CRP), interleukin-6 (IL-6), IL-10, tumor necrosis factor- α (TNF-α), and BMI. We used data from two sub-studies of the Adventist Health Study 2 cohort (Calibration, n = 893, and Biological Manifestations of Religion, n = 478) to test the hypothesis that vegetarian dietary patterns influence circulating levels of these biomarkers. The proportion of non-vegetarians, pesco- and semi-vegetarians, lacto-ovo vegetarians, and strict vegetarians in the analytic sample was 44%, 16%, 31%, and 9%, respectively. Non-vegetarians and partial vegetarians were older than other dietary groups. Blacks tended to be pesco- or non-vegetarians. In multivariable regression analysis, when comparing to non-vegetarians, IGF-1was higher in lacto-ovo vegetarians ($p = 0.04$) as was IGFBP-3 ($p = 0.01$). IGFBP-3 levels were also higher in partial vegetarians ($p = 0.001$). Insulin, CRP and BMI were significantly lower in each of the vegetarian dietary patterns compared to non-vegetarians. IL-10 in lacto-ovo and partial vegetarians were significantly lower than those of non-vegetarians. Significance persisted for IGFBP-3, insulin, CRP, and IL-10 after additional adjustment for BMI. IL-6 and TNF- α of strict, lacto-ovo, partial-, pesco- and semi-vegetarians were not statistically different from those of non-vegetarians. BMI and circulating levels of IGF-1, IGFBP-3, insulin, and CRP are biomarkers of higher cancer risk that may be modifiable by vegetarian diets.

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ASSOCIATION BETWEEN SERUM 25(OH) VITAMIN D, INCIDENT LIVER CANCER AND CHRONIC LIVER DISEASE MORTALITY IN THE LINXIAN NUTRITION INTERVENTION TRIALS: A NESTED CASE-CONTROL STUDY. *Jianbing Wang, Christian Abnet, Wen Chen, Sanford Dawsey, Jinhu Fan, Liangyu Yin, Jian Yin, Jacqueline Major, Philip Taylor, Youlin Qiao, Neal Freedman (National Cancer Institute, Rockville MD 20852)

Background: Although vitamin D deficiency has been noted in cross-sectional studies of chronic liver disease and laboratory studies suggest possible benefits of vitamin D in preventing liver cancer, little epidemiologic data is available. Methods: We prospectively examined the association between serum 25(OH) vitamin D and subsequent risk of liver cancer incidence or chronic liver disease mortality in the Linxian Nutrition Intervention Trials. Baseline serum 25(OH) vitamin D was measured for 226 incident liver cancer cases, 282 chronic liver disease deaths and 1063 age-, sex- and trial-matched controls. Unconditional logistical regression models were used to estimate odds ratios(OR) and 95% confidence intervals(CI). Results: The median serum 25(OH) vitamin D level in controls was low(20 nmol/L). Compared to the lowest quartile, subjects in the fourth quartile had lower risk of chronic liver disease death (OR = 0.34, 0.21 to 0.55), with a monotonic trend ($p < 0.001$). In lag analyses, this association remained statistically significant in participants with even over 14 years of follow-up. For liver cancer incidence, risk estimates were below one, but were not statistically significant overall. Associations, however, were significant among participants with higher serum calcium levels (Q4 vs Q1, OR = 0.43, 0.21 to 0.89). Results for chronic liver disease did not vary by serum calcium level. Conclusions: In a low vitamin D population, higher serum 25(OH) vitamin D concentrations were associated with significantly lower risk of chronic liver disease deaths, and among those with higher serum calcium, incident liver cancer. Our results suggest a possible protective role for vitamin D in these diseases.

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ASSESSING THE EFFECTIVENESS OF A CANCER SCREENING TEST IN THE PRESENCE OF ANOTHER SCREENING MODALITY IN NONRANDOMIZED STUDIES. *Jessica Chubak, Rebecca A Hubbard, Eric Johnson, Aruna Kamineni, Carolyn M Rutter (Group Health Research Institute, Seattle WA 98101)

Understanding how to analyze real-world screening data is important for studies of cancer where multiple screening modalities are common and the comparative effectiveness of different regimens has not been established. One modality of screening may confound the estimate of the effectiveness of another screening modality by reducing both the likelihood of receiving the screening test of interest for a period of time and reducing the risk of cancer mortality. This manuscript identifies and discusses alternative analytic approaches for analyzing data with multiple screening modalities, uses simulations to compare bias and efficiency across approaches, and makes recommendations on how to analyze the effectiveness of screening tests in the presence of other screening modalities or prior negative diagnostic exams. Simulated data are used to compare five analytic options: pooling, censoring, adjusting, stratifying, and excluding. The bias and precision of these approaches were investigated, varying the uptake rate of the competing screening modality among unscreened individuals and those previously screened with the modality of interest. For each scenario we simulated 1,000 cohorts of size 100,000. We considered the example of screening fecal occult blood tests (FOBT) as the exposure of interest with screening colonoscopy as the competing exam. Censoring at the time of colonoscopy was the only approach that was unbiased under all scenarios. Assuming that screening FOBT reduces the risk of colorectal cancer mortality by 11 deaths per 100,000 person-years, the other approaches overestimated the protective effect of screening FOBT by approximately 3 to 33/100,000 person-years overall and by 46 to 52/100,000 person-years among people who had received screening colonoscopy. Confounding arises in this setting because the only people who can be screened by both modalities are those whose first screening test was negative, and therefore are at lower risk of cancer mortality. Censoring at the competing exam is therefore the preferred approach.

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ESTIMATING THE INCIDENCE AND SEVERITY OF INFLUENZA IN THE UNITED STATES: A BAYESIAN PERSPECTIVE. *Carrie Reed, Sandra Chaves, Pam Daily Kirley, Ruth Emerson, Deborah Aragon, Emily Hancock, Lisa Butler, Gary Hollick, Matthew Laidler, Ann Thomas, Lyn Finelli (Centers for Disease Control and Prevention, Atlanta GA 30333)

Surveillance for influenza is challenging as only a fraction of all cases will seek medical care; an even smaller group will be tested and confirmed to have influenza. This complicates the ability to understand the full incidence and severity of an epidemic. During the 2009 pandemic, CDC developed a probabilistic model to correct surveillance data for biases in influenza ascertainment and estimate influenza-related health outcomes in the United States. Post-pandemic, we sought to further explore this methodology for annual estimation of the seasonal influenza disease burden. This analysis examined the use of a Bayesian synthesis approach to combine data from multiple sources and estimate the incidence of influenza hospitalization and the risk of death. We used data on laboratory-confirmed influenza hospitalization from the Emerging Infections Program and collected additional data on detection probabilities for hospitalization and death. Evidence, prior information, and associated uncertainty were analyzed in a Bayesian evidence synthesis framework. We estimated that surveillance detected 29-40% of influenza-associated hospitalizations and 17-27% of deaths in the surveillance catchment area, varying by age group. Geographic variability was also examined. When extrapolated to the US population, we estimated a total of 190,890 influenza-associated hospitalizations (95% credible interval: 173,250-210,860) and 7,460 (95% CI: 5,402-12,998) deaths from October 2010-April 2011. Future plans involve expanding the model to include outcomes such as illness, medically-attended illness, and intensive care admission. Exploring different methods to synthesize surveillance data and correct for biases can improve estimates of the annual influenza disease burden, which provide public health officials with necessary information to evaluate the impact of annual programs and allocate resources effectively.

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YEARS OF LIFE LOST IN THE FIRST WAVE OF 2009 PANDEMIC (H1N1) IN HONG KONG. *Ying Zhou, Eric Lau, Dennis IP, Hiroshi Nishiura, Gabriel M Leung, Wing Hong Seto, Benjamin J Cowling (School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, China., Hong Kong SAR China)

Background: The years of life lost (YLL) is an estimate of the life expectancy if a person had not died prematurely from influenza to measure of the impact of influenza pandemics. However, reported estimates of YLL have typically ignored the presence of underlying chronic conditions or health risk behaviors in most individuals who died and overestimated the remaining life expectancy. Methods: Data were available on individual patients in Hong Kong with laboratory-confirmed 2009 influenza A(H1N1) virus infection who died between May 2009 and March 2010. For confirmed deaths with underlying risk factors, the life expectancy was corrected with hazard-based modifications to the life tables. For each underlying risk factor, we obtained plausible estimates of the relative survival and converted these to excess hazards. The excess hazards were added to the 'baseline' age-specific hazards in the local life tables to reflect the life expectancy associated with the underlying risk factor. Results: There were 72 deaths among patients with laboratory-confirmed 2009 influenza A/H1N1 virus infection and 56% of deaths had underlying risk factors. We estimated that the 2009 pandemic was associated with 1540 (95% uncertainty range: 1350-1630) YLL adjusting for age and underlying risk factors. That was approximately 25% lower than the YLL estimate of 2,080 adjusted for age but not for risk factors. Adjustment for underlying risk factors led to substantial reductions in YLL estimates for older adults, and on average the YLL was reduced by a factor of 2 in individuals with underlying risk factors. Conclusion: We illustrated an estimation approach of YLL that accounts for underlying risk factors in addition to age. Our estimates of the YLL correcting for underlying risk factors provides a framework for similar calculations elsewhere.

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CASE FATALITY RISK OF 2009 PANDEMIC INFLUENZA A(H1N1): A SYSTEMATIC REVIEW AND META-ANALYSIS. Jessica Wong, Heath Kelly, Dennis Ip, Joseph Wu, Gabriel Leung, *Benjamin Cowling (The University of Hong Kong, Pokfulam Hong Kong SAR China)

Background: During the 2009 influenza pandemic, confusion over the severity of human infections with the H1N1pdm09 virus hindered the appropriate public health response. One measure of severity is the case fatality risk, defined as the probability of mortality among people classified as cases. Methods: We conducted a systematic review and meta-analysis to summarize published estimates of the case fatality risk of the influenza H1N1pdm09 virus. Results: We included 72 estimates of the case fatality risk from 46 published studies, around one-third of which were published before January 2010. We identified very substantial heterogeneity in published case-fatality risk estimates, ranging from less than 1 to greater than 10,000 per 100,000 infections. Choice of the denominator accounted for substantial heterogeneity, with much higher estimates of the case fatality risk based on confirmed case denominators compared to symptomatic case denominators or infection denominators. The point estimates of the case-fatality risk based on symptomatic case denominators increased substantially with age. Discussion: Some of the differences in estimates of the case fatality risk could be attributed to the differences in the definition of the denominators. Substantial variability in age-specific CFR estimates complicates the interpretation of the overall CFR and comparison between populations. It is essential to reach a consensus on how to define and measure the severity of a mild infectious disease before the next pandemic.

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MODELING THE POTENTIAL IMPACT OF AN INFLUENZA A/H3N2V VACCINE IN THE UNITED STATES. *Carrie Reed, Rebekah Borse, Manoj Gambhir, Matthew Biggerstaff, Martin I Meltzer, Lyn Finelli, Sonja Rasmussen, David Swerdlow (Centers for Disease Control and Prevention, Atlanta GA 30333)

In 2011, a novel influenza A/H3N2 variant virus (H3N2v) with swine origin was detected in humans. The new virus contained a gene from the 2009 H1N1 pandemic influenza virus which may have contributed to its increased transmissibility. Sustained human-to-human transmission of H3N2v was not seen, but given the virus' pandemic potential, a candidate vaccine virus was identified. In 2012, a larger outbreak of H3N2v in ten states prompted consideration of whether to produce H3N2v vaccine in readiness for distribution if sustained human transmission was observed. To provide information to decision-makers, we modeled the potential spread and health impact of an H3N2v epidemic in the US with and without a vaccination program. We combined epidemiologic information from the H3N2v investigation in an age-structured SEIR transmission model, varying the possible reproductive number (R) of the virus from 1.1-1.5. We then modeled the potential of H3N2v vaccination for averting illnesses, hospitalizations and deaths, assuming a base case of 16 weeks to vaccine availability, 62% vaccine efficacy, and vaccine coverage of 35-75% based on age. We estimated that without vaccination, 15-58 million illnesses, 150,000-650,000 hospitalizations, and 20,000-100,000 deaths could occur, with most occurring before the vaccine was available unless R = 1.1. Only a small fraction of outcomes (0.1-6.6%) would be averted by vaccine if the decision to produce vaccine was made after recognition of sustained transmission, the fraction decreasing as the value of R increased. Sensitivity analysis around the timing of vaccination indicated earlier vaccination would increase impact. The results highlight the need to invest in research that can reduce influenza vaccine production time. Further, our analysis represents a multidisciplinary effort to summarize epidemiologic information and mathematical models that can help inform policy makers during key public health decisions.

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PREDICTING INFLUENZA ADMISSIONS AMONG VETERANS FROM TELEPHONE TRIAGE. *Carla Winston, Cynthia Lucero-Obusan, Patricia Schirmer, Mark Holodniy (U.S. Department of Veterans Affairs, Palo Alto CA 94304)

Healthcare utilization and telephone triage data for 2010-2011 and 2011-2012 influenza seasons were obtained from national surveillance of 80 Veterans Affairs hospitals across the United States. Influenza-specific International Classification of Diseases 9th Revision codes were used to identify phone calls for which telephone triage recorded influenza as the primary concern and to define influenza-associated hospitalizations. We examined autocorrelation and cross correlation for autoregressive order and potential lags. After evaluating information criteria and model residuals to determine best fit, we compared three types of models for influenza hospitalizations based on telephone triage: 1) seasonal auto-regressive integrated moving average methods (SARIMA), 2) Poisson or negative binomial regression with sine and cosine terms for seasonality, and 3) Poisson regression with seasonal and lag terms. We used robust variance estimators and rounded all predictions to integer bounds. Weekly hospitalizations ranged 0–49; median 2, mean 6, variance 92. Weekly calls ranged 25–158; median 75, mean 77, variance 759. For the second-order SARIMA with 52 week seasonality, 29 (32%) of 92 weekly predictions included observed hospitalizations within 95% bounds. For Poisson with sine and cosine, 52 (57%) of 92 weekly prediction bounds were accurate. Negative binomial models with sine and cosine predicted 50 (54%) of 92 weeks. Adding a lag term to Poisson regression improved model fit statistics, but not accuracy, with 50 (55%) of 91 weeks accurate and no prediction for the first lag week. Poisson models with just sine and cosine had greater accuracy and smaller robust standard errors than other seasonal models. We will test models against 2012-2013 influenza data.

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THE PERILS OF COLLIDER STRATIFICATION: THE OBESITY PARADOX EXPLAINED. *Hailey R Banack, Jay S Kaufman (McGill University, Montreal QC Canada)

Several prospective studies have reported a J-shaped relationship between body mass index (BMI) and mortality, demonstrating an increased risk of death in the lowest and highest BMI groups. Although obesity is associated with a higher mortality risk in the general population, an "obesity paradox" has been reported among individuals with diabetes. We propose that this apparent paradox is simply the result of collider stratification, a well-known source of selection bias in epidemiologic research. Conditioning on a collider distorts the association between exposure and outcome among those selected for analysis and produces the spurious protective association between obesity and mortality among diabetics. The objective of this presentation is to demonstrate the magnitude of bias in the relationship between BMI and mortality induced by conditioning on diabetes status. Data from the 1999-2000 and 2000-2001 US National Health and Nutrition Examination Survey (NHANES) will be used. Among individuals with diabetes, the prevalence of obesity was higher than in the general population (55% vs. 41%). In the complete NHANES cohort, obesity was associated with an increased risk of mortality (OR = 1.67; 95% CI: 1.43, 1.96), however, in the sample stratified on diabetes status, a protective effect was observed (OR = 0.78; 95% CI 0.51, 1.19). Sensitivity analyses will be used to demonstrate the magnitude of selection bias induced by collider stratification under a range of simulated conditions. These analyses will elucidate the degree of bias required to reverse the direction of the observed association and highlight the perils of collider stratification bias.

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RACE OR PLACE? EXPLORING RACIAL MODIFICATION OF THE OBESITY GENDER GAP. *Marissa J Seamans, Whitney R Robinson, Roland J Thorpe, Thomas A LaVeist (University of North Carolina at Chapel Hill, Chapel Hill NC 27599)

In the U.S., black females have much higher obesity prevalence than black males; this gender inequality is not present in U.S. Whites. Although this racial difference has been attributed to genetics and race-specific culture, an alternative hypothesis is that racial differences in residence and socioeconomic status could account for the Black-White difference in (or racial modification of) the obesity gender gap. With directed acyclic graphs, we show that this hypothesis is tested using a novel study design that samples a racially integrated community with no race difference in income. We contrast racial modification of the obesity gender gap in the nationally representative 2003 National Health Interview Survey (NHIS) with that in the Exploring Health Disparities in Integrated Communities-Southwest Baltimore (EHDIC) study. EHDIC is a 2003 cross-sectional, population-based survey of adults in two low-income, racially integrated census tracts in Baltimore, MD (N = 1,408). In NHIS, the obesity gender gap was 9.5 percentage points (ppts) in non-Hispanic Blacks (37.9% women obese vs 28.4% men obese) and -1.8 ppts in non-Hispanic Whites (21.2% women vs 23.0% men). In NHIS, race modified the gender gap (Wald $p < 0.01$). In EHDIC, the age-standardized obesity gender gap was 15.5 ppts in Blacks (38.5% women vs 23.0% men) and 14.4 ppts in Whites (35.5% women vs 21.1% men). In EHDIC, there was little evidence of racial modification of the gender gap ($p = 0.83$). These results indicate that the obesity gender gap in Blacks is not genetically or culturally determined, but instead reflects racial differences in residential and socioeconomic exposures.

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HOW IS PREGNANCY-RELATED WEIGHT CHANGES AND BREASTFEEDING RELATED TO LONG-TERM MATERNAL WEIGHT AND WAIST CIRCUMFERENCE? A PATH ANALYSIS. *Helene Kirkegaard, Henrik Stovring, Kathleen M Rasmussen, Barbara Abrams, Thorkild I A Sorensen, Ellen A Nohr (Department of Public Health, Aarhus University, Aarhus C Denmark)

Pregnancy is related to excessive increase in a woman's weight and fat mass that may lead to long-term maternal weight gain and obesity. This study examined, by using a new statistical approach, how breastfeeding, gestational weight gain, postpartum weight retention at 6 months, and weight changes in early motherhood (6 to 18 months) were related to weight and waist circumference for given body mass index 7 years after birth. Women (n = 23,701) from the Danish National Birth Cohort with singleton births and no birth during follow-up were included. Information on anthropometry, breastfeeding duration, and covariates was obtained from interviews conducted at pregnancy week 16, at months 6 and 18 postpartum, and from a web-based-survey 7 years after birth. Using path analysis, we assessed the total, direct, and indirect effect mediated through weight changes on the pathway. Postpartum weight retention at 6 months ($p < 0.001$ for weight and $p = 0.04$ for waist circumference) and weight gain in early motherhood ($p < 0.001$ for both outcomes) were highly positively associated with both outcomes with 1 kg increase in weight retention at 6 months corresponding to an increase of 0.5 kg at 7 years. Gestational weight gain was not associated with waist circumference ($p = 0.47$), but positively associated with long-term weight ($p < 0.001$); 87% of this effect was indirect. For both outcomes, breastfeeding duration showed an inverse association ($p = 0.002$ for weight and $p < 0.001$ for waist circumference). It was strongest for waist circumference, where 97% of the effect was direct, that is, not mediated through postpartum weight loss. This finding suggests that breastfeeding may have a beneficial effect on fat distribution. Weight changes in the postpartum period and early motherhood contribute to long-term maternal weight gain.

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COMMUNITY SOCIOECONOMIC DEPRIVATION AND OBESITY TRAJECTORIES IN CHILDREN USING BIG DATA. *Claudia Nau, Thomas A Glass, Ann Y Liu, Jonathan Pollak, Brian S Schwartz (Johns Hopkins Bloomberg School of Public Health, Baltimore MD 21205)

Little is known about how community-level socioeconomic conditions alter trajectories of body weight gain in children. Using data from a large electronic health record, we investigate whether residence in communities with higher socioeconomic deprivation is associated with an obesogenic growth trajectory. Children ages 3-18 residing in a 37 county area of Pennsylvania with longitudinal measured weight and height (N = 161,771) were geocoded to 1289 communities. Socioeconomic deprivation was measured using a multidimensional scale and interpolated for inter-census years; each child was assigned the scale value nearest to their date of birth. Children living in communities in the highest quartile of socioeconomic deprivation were 36% more likely to at or above 85th percentile in body-mass index (BMI) (95% confidence intervals = 1.34-1.38) compared to those in the lowest quartile adjusting for age and sex. Random effects (growth curve) models were estimated accounting for differences in trajectories of BMI by age and sex. In models of change in BMI, correcting for non-constant residual variance across age groups, children living in communities with greater deprivation had higher BMI at first observation and steeper increase in BMI growth with age after adjustment for potential confounders. The best fitting model included linear, quadratic and cubic interactions between deprivation and age, suggesting a complex temporal pattern consistent with periods of heightened vulnerability to environmental influence. The association was not substantially attenuated after adjustment for a measure of individual deprivation. The association between deprivation and BMI did not vary by sex. Increased socioeconomic deprivation at the community level may be accelerating the obesity epidemic by altering the growth trajectory of body weight in early life. Electronic health records from large health care systems over diverse geographies offer important opportunities to examine dynamic population patterns using "big data".

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WEIGHT LOSS AND CORONARY HEART DISEASE AND ALL-CAUSE MORTALITY IN MIDDLE-AGED OR OLDER WOMEN: SENSITIVITY ANALYSIS FOR UNMEASURED CONFOUNDING BY UNDIAGNOSED DISEASE. *Goodarz Danaei, James Robins, Frank Hu, Jo Ann Manson, Miguel Hernan (Harvard School of Public Health, Boston MA 02115)

Several large meta-analyses of prospective studies have found a positive association between adiposity and both coronary heart disease (CHD) and all-cause mortality. However, the evidence on the effect of weight loss on these outcomes has been more mixed and there is a potential for unmeasured confounding due to undiagnosed diseases that may affect weight loss. We followed 73,318 women enrolled in the Nurses' Health Study from 1982 to 2008. Mean age at baseline was 48 and mean body mass index (BMI) was 24.5 kg/m2. We applied the parametric g-formula to estimate all-cause mortality and CHD incidence separately and conducted a sensitivity analysis for unmeasured confounding due to undiagnosed disease by imposing a lag time of 2-18 years between weight loss and the disease outcomes. During 26 years of follow-up, 2843 CHD events and 9202 deaths occurred. Results did not indicate a reduction in all-cause mortality or CHD incidence following various degrees of weight loss among overweight women (i.e. BMI >25 kg/m2). Changing the lag time and restricting the sample to never-smoking women or those with intentional weight loss did not change the results. Neither did excluding older women (age $\geq$ 70) and those with major chronic diseases from the intervention group. Weight loss, however, was associated with reduced incidence of type 2 diabetes after imposing a 6 year lag. The estimated reductions in risk of CHD with other lifestyle interventions such as quitting smoking, engaging in physical activity and drinking alcohol after imposing lag times of 2-18 years were smaller than the results without a lag time but were still statistically significant. We did not observe an expected reduction in CHD or all-cause mortality following weight loss in this cohort of US women. This may be due to residual confounding due to frailty or measurement error, or to a true lack of effect of weight loss in middle-aged or older women because of established atherosclerosis.

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SOCIAL INEQUALITY IN BREAST CANCER - QUANTIFICATION OF THE MEDIATING EFFECTS OF LIFESTYLE AND REPRODUCTIVE PATTERNS. *Ulla Hvidtfeldt, Theis Lange, Ingelise Andersen, Finn Diderichsen, Niels Keiding, Eva Prescott, Thorkild Soerensen, Anne Tjoenneland, Naja Rod (Department of Public Health, University of Copenhagen, Copenhagen Denmark)

Studying mechanisms underlying social inequality in breast cancer is important in order to develop prevention strategies. Based on a pooled cohort of 6 individual studies from the Copenhagen area including 33,562 women (1,733 breast cancer cases) aged 50-70 years at baseline, this study applied a new method for mediation analysis enabling the decomposition of the direct effect of socioeconomic position (measured by educational level) and indirect effects of reproductive and lifestyle factors on breast cancer. The total effect of socioeconomic position on breast cancer was 74 (95% confidence interval (CI): 22, 125) extra cases per 100,000 person-years for women with a long educational level compared to a short educational level. Of these, 26% (95% CI: 14%, 69%) could be attributed to a higher alcohol consumption. Similar effects were observed for age at first birth (32%; 95% CI: 10%, 257%), parity (19%; 95% CI: 10%, 45%), and hormone therapy use (10%; 95% CI: 6%, 18%). In conclusion, a substantial number of breast cancer events could be eliminated if women of high educational level changed their alcohol consumption, use of hormone therapy, and reproductive patterns corresponding to women of low educational level.

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ASSESSMENT OF MEDIATION BY BEHAVIORAL RISK FACTORS ON EDUCATIONAL-RELATED GRADIENTS IN CAUSE-SPECIFIC MORTALITY USING ADDITIVE HAZARDS MODELING: A MULTICENTER COHORT STUDY. *Helene Nordahl, Theis Lange, Birgitte Lidegaard Frederiksen, Merete Osler, Finn Diderichsen, Ingelise Andersen, Naja Hulvej Rod (Department of Public Health, University of Copenhagen, Copenhagen Denmark)

Quantitative assessment of the mediating effects of health behavior on educational-related gradients in mortality is crucial for prioritizing between such modifiable risk factors to tackle inequality in health. In this study we applied contemporary methods of additive hazards modeling to estimate the absolute number of cause-specific deaths per person-years (PY) due to educational level. We then decomposed the additional number of deaths attributable to the direct and indirect pathways through four behavioural risk factors among 76,000 women and men in the Danish Multicenter Social Inequality in Cancer Cohort Study from 1980 to 2009. Short educational level was associated with a total effect of 1270 (95% confidence interval = 1056;1484) and 725 (576;875) extra deaths per 100,000 PY at risk compared to long educational level for men and women, respectively. In men with short education 137 (116;160) cancer deaths, 87 (70;104) deaths from cardiovascular diseases, and 42 (33;51) deaths from respiratory diseases per 100,000 PY at risk could be ascribed to the pathways through smoking. Further, -17 (-38;4) cancer deaths, 76 (55;99) deaths from cardiovascular diseases, and -20 (-30;-9) deaths from respiratory diseases could be ascribed to pathways through BMI. Mediation by alcohol intake and low physical activity was marginal and did not vary in cause-specific mortality. Similar results were found for women. The results emphasize the importance of specifying the causes of death and the modifiable health behaviors when investigating socioeconomic inequality in mortality.

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THE ASSOCIATION BETWEEN SOCIOECONOMIC POSITION, MODIFIABLE RISK FACTORS AND HEART DISEASE INCIDENCE IN CANADA: THE NATIONAL POPULATION HEALTH SURVEY. *Brendan T Smith, Peter M Smith, Douglas G Manuel, Sam Harper, Cameron Mustard (Dalla Lana School of Public Health, University of Toronto, Toronto ON Canada)

The contribution of modifiable risk factors to social inequalities in heart disease in Canada is currently unclear. We examined the extent to which socioeconomic position (SEP) is association with heart disease incidence and the portion of the association mediated by modifiable risk factors. The National Population Health Survey includes over 17 years of biennial follow-up in a nationally representative cohort of Canadians (1994-2011). Multivariable Cox proportional hazards models were used to estimate the association between SEP (education, occupation and income) and self-report heart disease in respondents over 28 years and heart disease free at baseline (n = 9,337, 56% women). All analyses were adjusted for confounders (age, marital status, visible minority and immigration) with subsequent models adjusted for mediators (other SEP measures, body mass index, smoking, alcohol and physical activity). Education was inversely associated with heart disease in women (confounder-adjusted hazard ratio (HR) = 2.10, 95% confidence interval (CI):1.49,2.96), but not in men (confounder-adjusted HR = 1.13, 95% CI:0.87,1.47) when comparing respondents with less than secondary school graduation compared to university graduation. Similarly, both occupation (confounder-adjusted HR = 2.64, 95% CI:1.56,4.46 unskilled compared to professional) and income (confounder-adjusted HR = 1.84, 95% CI:1.31,2.58 lowest compared to highest quartile) were inversely associated with heart disease in women, but not men. All associations were attenuated when adjusting for mediators. The next steps will be to estimate the direct and indirect effects of SEP on heart disease through more sophisticated mediation modeling methods. The present study provides evidence of socioeconomic inequalities in heart disease incidence in Canadian women, but not men. A better understanding of the mediating pathways will provide targets for population health interventions to reduce social inequalities in heart disease.

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THE MOVING TO OPPORTUNITY EXPERIMENT AND ADOLESCENT PSYCHOLOGICAL DISTRESS: WERE EFFECTS MEDIATED BY NEIGHBORHOOD CHARACTERISTICS? *Theresa Osypuk, Quynh Nguyen, M Maria Glymour, Nicole Schmidt, Eric Tchetgen (University of Minnesota School of Public Health, Minneapolis MN 55454)

Motivation: Moving to Opportunity (MTO), a 5-city Randomized Controlled Trial offering low-income families rental housing vouchers to move out of public housing, had beneficial effects on mental health of girls, but harmful effects for boys. No studies have established mediators of these effects. Methods: MTO treatment group (n = 1950 adolescents receiving vouchers & 879 in-place controls) was the primary exposure predicting psychological distress (Kessler's K6). Neighborhood context, based on census tract of residence post-randomization, was characterized by 20 variables including: census-based neighborhood economic conditions (& 3 other census constructs, distilled by factor analysis), violent crime, neighborhood-level collective efficacy estimated from external population-based neighborhood surveys, and neighborhood quality reported at the individual level by MTO participants (i.e. neighborhood safety, collective efficacy, and disorder). In gender stratified analyses, we used regression based effect decomposition, after comparing results with Inverse Odds Weighting methods to confirm similar findings. Results: Participant-reported neighborhood safety, collective efficacy, and disorder (which improved for the MTO voucher group, both genders) partially mediated beneficial treatment effects on distress for girls, and exhibited countervailing mediation effects for boys. Yet no tested variables accounted for the harmful treatment effects on boys' distress. Though neighborhood economic conditions improved for the MTO voucher group, we unexpectedly found harmful indirect effects on distress for both genders. Crime, neighborhood-level collective efficacy, and other tested census constructs did not mediate. Conclusion: Although no neighborhood variables accounted for the majority of the total MTO effects on distress, housing mobility policy targeting some neighborhood improvements may in turn improve mental health for adolescent girls.

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THE BUILT ENVIRONMENT AS A MEDIATOR IN THE RELATIONSHIP BETWEEN RACIAL RESIDENTIAL SEGREGATION AND PRETERM BIRTH IN DURHAM, NORTH CAROLINA. *Rebecca Anthopolos, Lynne Messer, Jay Kaufman, Marie Lynn Miranda (School of Natural Resources and Environment, University of Michigan, Ann Arbor MI 48109)

Background. While racial residential segregation has been associated with preterm birth, few studies have examined potential mediating pathways. An obstacle to mediation analysis with a binary outcome like preterm birth is that indirect effects estimated from multiplicative models generally lack causal interpretation. We develop a novel method to estimate additive scale natural direct and indirect effects from logistic regression. We use our method to evaluate whether segregation operates through the built environment to impact preterm birth. Methods. We derive risk differences (RDs) from logistic regression coefficients in order to estimate natural direct and indirect effects. Birth records (2000-2008) for Durham, NC, were linked to neighborhood-level measures of racial isolation and seven domains of the built environment. We decomposed the total effect of racial isolation on preterm birth into direct and indirect effects through each built environment measure. Results. The adjusted total effect of an interquartile (IQR) change in racial isolation on preterm birth risk was an extra 27 preterm events per 1,000 births (RD = 0.027, 95% CI: 0.007, 0.047). With housing damage, property disorder, renter occupancy, and vacancy at their level under isolation at the 25th percentile, the direct effects of an IQR change in isolation were 0.024 (95% CI: 0, 0.044), 0.024 (95% CI: 0, 0.045), 0.022 (95% CI: 0, 0.042), and 0.021 (95% CI: -0.001, 0.040), respectively. Renter occupancy, vacancy, and nuisances accounted for 23, 17, and 16% of the total effect, respectively. Conclusions. Our methodology maintains an additive scale in natural effects estimation with a binary outcome. The majority of the total effect of racial isolation on preterm birth risk is direct, with small signals of indirect effects through specific measured domains of the built environment.

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PSYCHOSOCIAL STRESS AND RISK OF UTERINE LEIOMYOMATA IN BLACK WOMEN. *Lauren Wise, Se Li, Julie Palmer, Lynn Rosenberg (Slone Epidemiology Center, Boston University, Boston MA 02467)

Emerging research suggests that exposure to psychosocial stress increases risk of uterine leiomyomata (UL). UL are a major source of gynecologic morbidity in black women. We assessed the association between various measures of stress in adulthood and UL incidence among 23,527 premenopausal participants in the Black Women's Health Study, a prospective cohort study. Women were asked about perceived stress in 2005 (PSS-10 scale), depressive symptoms in 1999 and 2005 (CES-D scale), and caregiver responsibilities in 1995 and 2011. Biennial follow-up questionnaires from 1997 through 2011 identified new UL diagnoses. Age- and period-stratified Cox regression models were used to derive incidence rate ratios (RR) and 95% confidence intervals (CI) adjusted for lifestyle, anthropometric, and reproductive factors. During 1997-2011, there were 7,861 incident cases of UL confirmed by ultrasound or surgery. During follow-up from 2005-2011, RRs for PSS-10 scores of 9-12, 13-16, 17-20, and ≥21 (high stress) relative to <9 (low stress) were 1.14 (95% CI = 0.97-1.34), 1.02 (95% CI = 0.87-1.21), 1.16 (95% CI = 0.98-1.36), 1.22 (95% CI = 1.04-1.43), respectively (P-trend = 0.02). During follow-up from 1999-2011, RRs for CES-D scores of 16-24 and ≥25 (high depressive symptoms) relative to <16 (low depressive symptoms) were 1.11 (95% CI = 1.03-1.20) and 1.19 (95% CI = 1.09-1.31), respectively (P-trend < 0.001). Risk was also elevated for women with a history of clinical depression (RR = 1.22, 95% CI = 1.12-1.33). There was little evidence of an overall association between caregiving responsibilities (1995) and UL risk (RR = 1.06, 95% CI = 1.00-1.13). However, in cross-sectional analyses of 2011 data, caregiving perceived as "high stress/low reward" was associated with a 12% increased risk of UL (95% CI = 1.01-1.24) relative to "low stress/high reward" caregiving. Our data indicate a positive association of perceived stress, depression, and caregiver stress with incident UL in black women.

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PHYSICAL AND SEXUAL ABUSE VICTIMIZATION IN CHILDHOOD OR ADOLESCENCE AND RISK OF GESTATIONAL DIABETES. *Susan Mason, Deirdre Tobias, Cuilin Zhang, Frank Hu, Janet Rich-Edwards (Harvard Medical School, Boston, MA 02115)

Background: Abuse victimization has been linked to a variety of chronic disease outcomes in adulthood. In a recent study, we found that women who were physically or sexually abused in childhood had a substantially increased risk of type 2 diabetes in middle age. Women with abuse histories may also have an increased risk of gestational diabetes mellitus (GDM), a pregnancy condition with shared metabolic characteristics, but no published studies have examined this association. We investigated the relationship between childhood abuse victimization and risk of GDM in the Nurses' Health Study II (NHSII). Methods: In 2001, NHSII participants were asked about their experiences of physical and sexual abuse in childhood. A detailed pregnancy history, including the diagnosis of GDM in each pregnancy, was included in the 2009 NHSII questionnaire. We used a modified Poisson regression approach with generalized estimating equations to estimate risk ratios (RRs) and 95% confidence intervals (CIs) for GDM, as a function of severity of childhood physical and sexual abuse victimization. Results: Of 45,550 women included in the analyses, 8% reported severe physical abuse, and 5% reported multiple experiences of forced sexual activity in childhood or adolescence. Approximately 5% had one or more pregnancies complicated by GDM. In models adjusted for childhood socioeconomic variables, childhood body size, and family history of diabetes, severe physical abuse was associated with a 52% increase in GDM risk (RR = 1.52; 95% CI: 1.32, 1.75). More than one experience of forced sexual activity was associated with a 30% increase in GDM risk (95% CI: 1.08, 1.56). Compared to women without a history of abuse, women with a history of sexual abuse in addition to severe physical abuse were found to have a 77% increase in risk of developing GDM (RR = 1.77; 95% CI: 1.48, 2.12). Conclusion: Childhood abuse victimization is associated with increased risk of GDM in adulthood.

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PERSONALITY AND BIRTH OUTCOMES AMONG ADOLESCENTS.

*Emily Harville, Aubrey Spriggs Madkour, Yiqiong Xie (Tulane University, New Orleans LA 70112)

Background: Adolescent mothers as a group have worse birth outcomes than adult women, but the factors that predict birth outcomes within this adolescent group are not well characterized. Personality is known to be related to a number of health outcomes, but its relationship with birth outcomes has not been well studied. Methods: Data from the National Longitudinal Study of Adolescent Health were used. Participants were 938 adolescent girls who reported on pregnancy outcomes throughout their teenage years. Personality data was taken from the Mini-IPIP personality tool, administered at wave IV, which measures a five-factor personality traits of neuroticism, conscientiousness, intellect/imagination, extraversion, and agreeableness. Linear regression was used to predict birthweight and gestational age with adjustment for confounders. Data were stratified on race to examine possible cultural differences. Results: Higher neuroticism was associated with lower birthweight and gestational age among black girls, but not non-Black. Conscientiousness was associated with lower gestational age among non-Black girls in multivariable analysis. There were weaker tendencies for intellect/imagination to be associated with lower gestational age and conscientiousness to be associated with higher birthweight in Black girls. No relationships were found with extraversion or agreeableness. Conclusions: Personality and race interact to predict birth outcomes in adolescents?

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STRESSFUL EVENTS IN PREGNANCY AND POSTPARTUM DEPRESSIVE SYMPTOMS IN MASSACHUSETTS.

*Sarah Stone, Hafsatou Diop, Eugene Declercq, Howard Cabral, Lauren Wise (Boston University School of Public Health, Westwood MA 02090)

Background: The influence of perinatal stressors on the risk of postpartum depressive symptoms (PDS) is uncertain. We investigated the association between perinatal stressors and prevalence of PDS. Methods: We used the Massachusetts Pregnancy Risk Assessment Monitoring System (PRAMS) 2007-2010 data to evaluate whether perinatal experiences of selected stressors were associated with PDS and with subsequent help-seeking behaviors. We categorized 12 stressors into 4 groups: partner, trauma, financial and emotional. We defined PDS as report of 'always' or 'often' to any depressive symptoms; reference group reported 'sometimes', 'rarely' or 'never' to all depressive symptoms. Modified Poisson regression models directly estimated prevalence ratios (PRs) and 95% confidence intervals (CIs), controlling for socioeconomic status indicators, pregnancy intention and prior mental health visits. Results: Of the 5,375 participants in PRAMS during 2007-2010, 59% reported $\geq$1 stressor (partner = 26%, trauma = 16%, financial = 29% and emotional = 30%, weighted using SUDAAN). Report of $\geq$1 stressor was associated with an increased prevalence of PDS (PR = 2.77, 95% CI 2.18-3.50). Strongest associations were observed for partner stress (PR = 2.74, 95% CI 2.01-3.75), then trauma (PR = 1.83, 95% CI 1.17-2.88), financial (PR = 1.83, 95% CI 1.31-2.60) and emotional (PR = 1.44, 95% CI 1.02-2.03). Among those with PDS, there was little evidence that any type of stressor predicted help-seeking behavior. Conclusions: Life stressors during pregnancy were associated with increased prevalence of PDS; however, life stressors did not appreciably predict help-seeking behavior among women with PDS. Women should be screened in the perinatal period for stressors, and encouraged to seek help for effective primary prevention of PDS.

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RISK FACTORS ASSOCIATED WITH TRAJECTORIES OF FATHERS' DEPRESSIVE SYMPTOMS ACROSS THE EARLY PARENTING PERIOD: AN AUSTRALIAN POPULATION BASED LONGITUDINAL STUDY.

*Rebecca Giallo, Fabrizio D'Esposito, Amanda Cooklin, Daniel Christensen, Jan Nicholson (Parenting Research Centre, East Melbourne Victoria Australia)

Background: Fathers' are at heightened risk of depressive symptoms in the first year after having a baby. However, little is known about the course and persistence of depressive symptoms, and associated risk factors beyond the postnatal period. The aims of the study were to: (a) report on the course of depressive symptoms over the early parenting period (when children were aged 0-7 years) for a nationally representative sample of Australian fathers (b) identify classes of fathers defined by their trajectory of symptoms over time, and (c) identify early postnatal risk factors associated with persistent symptoms. Methods: Data from 2470 fathers participating in the Longitudinal Study of Australian Children were analysed. Latent growth class analysis was conducted to identify classes defined by distinct trajectories of depressive symptoms, and logistic regression conducted to identify risk factors associated with class membership. Results: The latent growth model for the overall sample revealed that fathers' depressive symptoms were highest during the first postnatal year and then gradually decreased across the early parenting period. However, the latent growth class analysis identified two distinct trajectories across the early parenting period. The majority of fathers (92%) reported moderate depressive symptoms in the first postnatal year and these decreased over time, whilst 8% of fathers reported high depressive symptoms during the first postnatal year and these tended to increase markedly over time. Early risk factors for persistent and increasing depressive symptoms were poor relationship quality, poor job quality, lower parental self-efficacy, and poor maternal postnatal mental health. Conclusion: A small proportion of fathers are at risk of persistent depressive symptoms across the early parenting period. The early risk factors identified in this study can inform approaches to the early identification, prevention and intervention for fathers at risk.

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.6RANDOMIZED CLINICAL TRIAL OF PRECONCEPTION LOW DOSE ASPIRIN USE TO IMPROVE PREGNANCY OUTCOMES: EAGER (EFFECTS OF ASPIRIN IN GESTATION AND REPRODUCTION) TRIAL.

*Enrique Schisterman, Robert Silver, Laurie Lesher, David Faraggi, Jean Wactawski-Wende, Janet Townsend, Anne Lynch, Neil Perkins, Sunni Mumford, Noya Galai (Eunice Kennedy Shriver National Institute of Child Health and Human Development, Rockville MD 20852)

Low dose aspirin (LDA) initiated post conception has had conflicting results on pregnancy outcomes. As preconception LDA may affect endometrial vascularization and placentation, post conception LDA initiation may miss the critical window for intervention. This multi-site prospective randomized double-blind placebo-controlled trial sought to determine whether preconception LDA (81 mg/day) treatment improves live birth rates in women with 1-2 prior losses. Women aged 18-40 actively trying to conceive were stratified as: 1) restricted: women with 1 documented loss <20 wks gestational age (GA) during the past year, or 2) general: women with 1-2 prior losses regardless of GA or time since loss. Randomization was stratified by site and restricted/general strata. Participants were treated/followed for 6 menstrual cycles or if they conceived, throughout pregnancy with treatment discontinued at 36 wks GA. An intent-to-treat approach with sensitivity analysis for compliance was used to estimate effects.1228 women were randomized: 615 LDA and 613 placebo. 1078 (87.8%) women completed the trial. Live birth rates were 57.8% LDA vs. 52.7% placebo ($p = 0.093$). In the restricted strata ($n = 492$), live birth rate was 62.4% LDA vs. 53.2% placebo ($p = 0.039$), and in the general strata ($n = 586$), 53.9% LDA vs. 52.2% placebo ($p = 0.68$). LDA was associated with higher implantation rates in the restricted strata (73.5% clinically confirmed pregnancies vs. 63.4% placebo), but not the general strata (66.0% LDA; 63.2% placebo). Major complications were similar among groups although LDA was associated with increased minor vaginal bleeding not associated with pregnancy loss. Daily LDA initiated preconception was associated with a significant increase in live births among women with a documented loss <20 wks GA during the past year.

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CERVICAL SURGERY FOR CERVICAL INTRAEPITHELIAL NEOPLASIA AND PROLONGED TIME TO CONCEPTION OF A LIVE BIRTH: A CASE-CONTROL STUDY. *C N Spracklen, K K Harland, B J Stegmann, A F Saftlas (University of Iowa, Iowa City IA 52242)

Possible mechanisms by which removal of cervical tissue could lead to sub-fertility include the disruption of cervical mucus production and cervical stenosis. To determine whether women with a history of prior cervical surgery for cervical intraepithelial neoplasia (CIN) are at increased risk of sub-fertility, measured as time to pregnancy of more than 12 months, we analyzed data from the Iowa Health in Pregnancy Study, a population-based case-control study of preterm and small-for-gestational-age, live birth outcomes (5/2002-5/2005). The analysis included women with an intended pregnancy and a history of one prior cervical surgery (n = 152), colposcopy-only (n = 151), or no prior history of cervical surgery or colposcopy (n = 1021). Cervical treatment history, pregnancy intention, time to pregnancy, and other variables were self-reported by computer-assisted telephone interviews. Odds ratios (OR) were calculated using logistic regression to estimate the risk of prolonged time to pregnancy (ie, >1 year) among women with a history of cervical surgery or colposcopy alone compared to untreated women (referent group). Prolonged time to pregnancy was most prevalent among treated women (16.4%) compared to untreated women (8.4%) and women with colposcopy only (8.6%) (p = 0.04).After adjusting for covariates, women with a prior cervical surgery had a two-fold higher risk of prolonged time to pregnancy compared to untreated women (adjusted OR = 2.09, 95% confidence interval (CI) 1.26-3.46). In contrast, women with a history of colposcopy-only had a risk equivalent to that among untreated women (adjusted OR = 1.02, 95% CI 0.56-1.89). These results suggest that women with a history of cervical treatment for CIN are at increased risk of sub-fertility.

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CYCLE-SPECIFIC PHTHALATE MEASURES, EARLY PREGNANCY LOSS AND TIME TO PREGNANCY. *Anne Marie Jukic, Clarice Weinberg, Jane Hoppin, Mattew Longnecker, Donna Baird, Allen Wilcox (National Institute of Environmental Health Sciences, Durham NC 27709)

Rodent studies suggest that phthalates are reproductive toxicants. A recent study found a strong association between high levels of monoethylhexyl phthalate (MEHP) in women and early pregnancy loss (Environ Health Perspect, 2012, 120:458-463). There are few opportunities to test for replication. We used data from the North Carolina Early Pregnancy Study (EPS) (1982-86) to examine the association of urinary phthalate metabolites with early pregnancy loss. In the EPS, women discontinuing contraception collected daily urine specimens and reported menstrual bleeding and sexual intercourse. Urine specimens were analyzed for estrogen and progesterone metabolites and human chorionic gonadotropin. Early pregnancy loss was defined as a loss prior to 6 weeks of gestation. Phthalate metabolites were measured in a pooled urine sample drawn from three separate daily specimens across each menstrual cycle. Creatinine-adjusted phthalate metabolite measures were divided into tertiles. Odds ratios for early loss were estimated with a logistic regression. The median MEHP level in our study was 6.7 ng/ml. (interquartile range 4.0, 11.1). There were 150 clinical pregnancies, and 48 early pregnancy losses. We saw no association of MEHP with early pregnancy loss (for the two highest tertiles compared with the lowest, odds ratio for early loss (CI): 1.7 (0.7, 4.5), 1.1 (0.4, 2.9) p = 0.4). To pursue the possibility of reproductive toxicity further, we also considered the number of ovulatory cycles required to achieve pregnancy (N = 711, 1-9 per woman). We estimated fecundability ratios with log linear regression. There was no evidence of reduced fecundability with MEHP exposure (two highest tertiles, fecundability ratios (CI) 1.3 (0.9, 1.9), 1.7 (1.1, 2.6) p = 0.9). (A ratio above one suggests higher fecundability.) Results for other measured phthalate metabolites were also negative. In sum, we found no evidence of detrimental phthalate effects on fertility.

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FECUNDABILITY IN WOMEN BORN PRETERM. *Cathrine Wildenschild, Anders H Riis, Vera Ehrenstein, Elizabeth Hatch, Lauren A Wise, Kenneth J Rothman, Henrik T Sorensen, Ellen M Mikkelsen (Aarhus University Hospital, Department of Clinical Epidemiology, Aarhus N Denmark)

An estimated 6-15% of pregnancies result in a preterm birth. Infants born preterm are at increased risk of adverse health outcomes, which may persist in adult life. Studies have found that women born preterm may have a decreased probability of giving birth, but precise data on the cycle-specific probability of conception (fecundability) in such women are lacking. We examined the fecundability of women born preterm in a prospective cohort study of 2,814 Danish pregnancy planners. Self-reported prospectively collected data on time to pregnancy were supplemented by data on gestational age obtained from the Danish Medical Birth Registry. We estimated fecundability ratios (FR) and 95% confidence intervals (CI) for women born preterm (<37 weeks), and women born postterm (≥42 weeks), relative to women born at term (37 weeks to 41 weeks 6 days) using proportional probabilities regression models. Relative to women born at term, the FRs were 0.87 (95% CI 0.66;1.13) for women born preterm, and 1.09 (95% CI 0.93;1.28) for women born postterm. After adjustment for birth year, weight at birth, and participant' mother' socio-demographic, medical and reproductive characteristics, the FRs were 0.91 (95% CI 0.68;1.24) for women born preterm and 1.09 (95% CI 0.93;1.28) for women born postterm. Our data do not support the hypothesis that being born preterm is associated with a decrease in fecundability.

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LOW TECHNOLOGY ASSISTED REPRODUCTION AND PRETERM BIRTH. *Carmen Messerlian, Seang Lin Tan, Robert Platt, Robert Gagnon, Olga Basso (McGill University, Montreal QC Canada)

A higher risk of preterm birth has consistently been observed among singleton pregnancies conceived through in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). The evidence regarding treatment that does not involve gamete manipulation, such as intrauterine insemination (IUI) is, however, limited. Low technology treatment could also conceivably be associated with adverse outcomes as even pregnancies occurring naturally after a period of infertility are at increased risk of preterm birth. We present preliminary results from a retrospective hospital-based cohort study of women residing in Montreal, Canada who delivered at the Royal Victoria Hospital from April 2001 to September 2007. We use the McGill University Obstetrical and Neonatal Database. The cohort consisted of 18,179 singleton births; of these, 110 were conceived through IUI or intra-cervical insemination (IUI group), 394 through IVF or ICSI (IVF group), and 17,675 had no indication of being conceived as a result of infertility treatment and served as the reference group. Crude odds ratios of preterm birth (≤37 weeks) were 1.99 (95% Confidence Interval (CI): 1.15-3.43) and 1.87 (95% CI: 1.38-2.54) for the IUI and IVF groups, respectively. Adjusting for age, parity, and education did not materially change estimates: 2.00 (95% CI: 1.15-3.48) and 1.80 (95% CI: 1.32-2.45) for the IUI and IVF groups, respectively. The adjusted odds ratios of very preterm birth (<34 weeks) were 4.36 (95% CI: 2.08-9.13) for the IUI group and 2.08 (95% CI: 1.22-3.53) for the IVF group. These results suggest that women undergoing low technology treatment are also at increased risk of preterm birth. It is possible that the underlying conditions leading to infertility may be involved in the etiology of adverse pregnancy outcomes.

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POWER AND SAMPLE SIZE CALCULATIONS FOR MENDELIAN RANDOMIZATION STUDIES. Guy Freeman, *Benjamin Cowling, Mary Schooling (The University of Hong Kong, Pokfulam Hong Kong SAR China)

Mendelian randomization, which is instrumental variable analysis using genetic variants as instruments, is an increasingly popular method of making causal inferences from observational studies. In order to design efficient Mendelian randomization studies, it is essential to calculate the sample sizes required. We present formulas for calculating exactly the power of a Mendelian randomization study to detect an effect of a given size and the minimum sample size required to detect effects for given levels of significance and power under certain common assumptions. We apply the formulas to some example data and compare the results to those from the usual simulation methods. Exact power and sample size calculations using these formulas should be more straightforward to carry out than simulation approaches and therefore facilitate appropriate study designs. Moreover, these formulas make explicit that the sample size needed for a Mendelian randomization study is inversely proportional to the square of the correlation between the genetic instrument and the exposure as well as the square of the effect size and the variance of the exposure, and proportional to the residual variance of the outcome once adjusted for the effect of the exposure.

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DIRECT EFFECT OF BIRTH WEIGHT ON CHILDHOOD BLOOD PRESSURE: A CAUSAL MEDIATION ANALYSIS. *Arnaud Chiolero, Gilles Paradis, Jay S Kaufman (University of Lausanne & McGill University, Switzerland & Canada)

Background: Numerous studies have shown a negative association between birth weight (BW) and blood pressure (BP) later in life. To estimate the direct effect of BW on BP, it is conventional to condition on current weight (CW). However, such conditioning can induce collider stratification bias in the estimate of the direct effect. Objective: To bound the potential bias due to U, an unmeasured common cause of CW and BP, on the estimate of the (controlled) direct effect of BW on BP. Methods: Data from a school based study in Switzerland were used (N = 4,005; 2,010 B/1,995 G; mean age: 12.3 yr [range: 10.1-14.9]). Measured common causes of BW-BP (SES, smoking, body weight, and hypertension status of the mother) and CW-BP (breastfeeding and child's physical activity and diet) were identified with DAGs. Linear regression models were fitted to estimate the association between BW and BP. Sensitivity analyses were conducted to assess the potential effect of U on the association between BW and BP. U was assumed 1) to be a binary variable that affected BP by the same magnitude in low BW and in normal BW children and 2) to have a different prevalence in low BW children and in normal BW children for a given CW. Results: A small negative association was observed between BW and BP [beta: -0.3 mmHg/kg (95% CI: -0.9 to 0.3)]. The association was strengthened upon conditioning for CW [beta: -1.5 mmHg/kg (95% CI: -2.1 to -0.9)]. Upon further conditioning on common causes of BW-BP and CW-BP, the association did not change substantially [beta: -1.4 mmHg/kg (95% CI: -2.0 to -0.8)]. The negative association could be explained by U only if U was strongly associated with BP and if there was a large difference in the prevalence of U between low BW and normal BW children. Conclusion: The observed negative association between BW and BP upon adjustment for CW was not easily explained by an unmeasured common cause of CW and BP.

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MULTIPLY ROBUST ESTIMATION OF TOTAL EFFECTS IN MULTILEVEL MODELS. *Maral DerSarkissian, Onyebuchi A Arah (Department of Epidemiology, University of California Los Angeles Fielding School of Public Health, Los Angeles CA 90095)

Hierarchical, or multilevel, data are becoming common in epidemiology as data are collected on participants from multiple neighborhoods, schools, healthcare facilities, cities, countries, etc. Multilevel models are needed to analyze such data in order to take into account the clustered hierarchical structure while estimating random or fixed effects. Confounding can exist at the group (i.e. contextual) level and at the individual (i.e. compositional) level in hierarchical data. Multiply robust estimation is a novel technique that affords investigators with more than two chances to specify a model correctly via a union of (sub-)models, obviating multiple results presentation. We demonstrate how multiply robust estimation combines three or more estimators in one multilevel union model to yield unbiased effect estimates provided at least one sub-model is correctly specified with regards to confounding control, no new bias is introduced, and there is no uncontrolled confounding given the measured set of confounding variables. We used Monte Carlo simulations to examine the causal effect of a binary exposure on a continuous outcome given contextual and compositional confounders. We combined inverse probability of treatment weighted fitting of marginal structural models, propensity score covariate adjustment, and outcome regression in our union model. We examined the performance of multiply robust estimation under different model specification scenarios. We evaluated its bias, variance, and coverage. Our results showed that effect estimates for the exposure were unbiased in all scenarios, provided at least one sub-model was correctly specified and regardless of which sub-model was misspecified. Our results support multiply robust estimation as a sophisticated method that investigators can use to hedge their bets on obtaining valid effect estimates from hierarchical data by using a union model.

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EFFICIENT DESIGN FOR MENDELIAN RANDOMIZATION STUDIES: SUBSAMPLE AND TWO-SAMPLE INSTRUMENTAL VARIABLE ESTIMATORS. *Brandon Pierce, Stephen Burgess (University of Chicago, Chicago IL 60637)

Mendelian randomization (MR) is a method for estimating the causal relationship between an exposure and an outcome using a genetic factor as an instrumental variable (IV) for the exposure. In the traditional MR setting, data on the IV, exposure, and outcome are available for all participants. However, obtaining complete exposure data may be difficult in some settings, due high measurement costs or lack of appropriate bio-specimens. The authors use simulated datasets to assess power and bias for MR estimation when exposure data are available for a subset (or an independent set) of participants. We show that obtaining exposure data for a subset of participants is a cost-efficient strategy, often having negligible effects on power compared to a traditional complete-data analysis. The size of the subset needed to achieve maximum power depends on IV strength, and maximum power is approximately equal to the power of the "reduced form" and traditional IV estimators. Weak IVs are shown to lead to bias towards the null when the subsample is small and towards the confounded association when the subset is relatively large. Various approaches for confidence interval calculation are considered. Due to the costs of large-scale biomarker measurement, these results have important implications for reducing the costs and increasing the feasibility of MR studies.

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FAMILIALITY OF SOCIAL RESPONSIVENESS SCALE SCORES IN THE NURSES' HEALTH STUDY II. *Kristen Lyall, Susan Santangelo, John Constantino, Andrea Roberts, Marc Weisskopf, Alberto Ascherio (University of California Davis, Oakland, CA 94610)

The Social Responsiveness Scale (SRS) is a widely used measure of autistic traits and social functioning. The goals of this study were to determine familiality of SRS scores in families with and without a child with an autism spectrum disorder (ASD), and to examine scores in association with previously identified risk factors for ASD. Participants were 470 cases and 1,647 controls from a nested case-control study within the Nurses' Health Study II. Pearson correlation coefficients, t-tests, and logistic regression adjusted for potential confounders were used to examine associations. Case fathers had significantly higher SRS scores than control fathers ($p < .0001$). Parent scores were correlated in both cases and controls (r in total study group = .32), suggesting assortative mating. Parent elevated scores in controls were associated with significantly higher child scores ($p < .0001$) relative to those with parent scores in the lower 80% of the distribution, corresponding to a shift in child raw score of ~15 points. Elevated scores in case parents were not associated with increases in child scores, though case parents were significantly more likely to have concordantly elevated scores (both parents in top 20% of distribution) than were control parents ($p = 0.0008$; adjusted odds ratio for parent concordantly elevated scores comparing cases to controls = 2.09, 95% CI 1.22, 3.59). Maternal depression was associated with increased mother and child SRS scores; other risk factors were not associated with scores. In models adjusting the previously identified risk factors for parental SRS scores associations were somewhat attenuated. Our results demonstrate familiality of autistic traits, as measured by the SRS, and suggest associations in this cohort with previously identified ASD risk factors are not largely impacted by parental broader autism phenotype.

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PARENTAL EARLY-LIFE SOCIOECONOMIC STATUSES AND CHILDHOOD BEHAVIOR PROBLEMS: WHAT ARE THE PATHWAYS? *Naoki Kondo, Misato Takada, Hideki Hashimoto (The University of Tokyo, Bunkyo-ku Tokyo Japan)

Objectives: To understand the pathways in the intergenerational transmission of health disparities, we evaluated the associations of parents' early-life and adult socioeconomic statuses (SES) and behavior problems of children. We sought to separate two potential pathways linking parental early-life SES to behavior problems, namely, social trajectories (mediated by adult SES) and latent-effects (parental biological embodiment of SES). Methods: We used 2010/11 baseline survey data of Japanese Study on Stratification, Health, Income, and Neighborhood (JSHINE). In this survey computer-assisted interviews were carried out for randomly selected families of four cities in Japan. We used data of 1,972 children aged between 4 and 17 years. Response rate was 67%. Behavior problems were evaluated using Strengths and Difficulty Questionnaire. Measures of parents' adult SES include household income, individual incomes, occupations, and educational attainments. Parents also reported their early-life SES in terms of perceived household economic conditions at the ages of 5 and 15 and their parents' educational attainments and occupation. We calculated prevalence ratios (PR) of middle or higher levels of behavior problems. Results: Mothers' education showed a higher PR than fathers'. In social trajectories models (adjusting for ages, parents' history of psychiatric disorders, problems during delivery, and low birth weights), PRs were 1.34 and 1.58 for low vs. high educational attainments of grandmothers on the fathers' and mothers' sides, respectively. Parents' household economic conditions at 5, but not at 15, were also strongly associated with behavior problems. In latent-effects models, further adjustment for current SES attenuated these associations but they remained statistically significant. Conclusion: Both social trajectories and latent effects may be likely. SES of mothers and grandmothers may more strongly affect psychological development.

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PERINATAL RISK FACTORS FOR AUTISM: FINDINGS FROM THE COLLABORATIVE PERINATAL PROJECT. *Emma Viscidi, Elizabeth Triche, Eric Morrow, Stephen Buka (Brown University, Providence RI 02903)

Autism is a neurodevelopmental disorder that is estimated to affect as many as 1 in 88 children. While there is evidence that genetic and environmental factors contribute to autism risk, the exact causes are unknown. Many studies have reported associations between perinatal factors and autism, but results have been inconsistent. Prospective cohort studies of autism are rare, but are the ideal means to investigate early life risk factors for autism. The Collaborative Perinatal Project (CPP) was a population-based cohort study of approximately 42,000 women and 51,000 children born in the US in the 1960s. Mothers were examined during pregnancy, labor, and delivery. Offspring were followed from birth to 7 years. The CPP has prospectively collected data on a large and diverse population of children in the US and is therefore an ideal cohort in which to study perinatal risk factors for autism. Autism was considered a rare disorder through the 1980s and, as such, the CPP study did not collect diagnostic information on autism. The objectives of the study were to: 1) retrospectively apply current diagnostic criteria to identify children with autism; and 2) examine perinatal risk factors for autism. Children with autism were identified by a diagnostic algorithm based on current diagnostic criteria for Autistic Disorder. Information on autism symptoms was drawn from psychological, physical, cognitive, and developmental evaluations. Out of 51,235 children in the cohort, 308 (0.6%) met criteria for autism. Multivariate regression models were used to examine the association between perinatal risk factors and autism. Preliminary results replicate prior findings (e.g. being small for gestational age, low apgar score, and older paternal age at birth were associated with increased risk of autism) and suggest new risk factors (e.g. mothers with hypertension at more than one prenatal visit had 1.49 times the odds of having a child with autism (95% CI: 1.10-2.03)).

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THE RELATIONSHIP BETWEEN RACE/ETHNICITY AND MAJOR BIRTH DEFECTS IN THE UNITED STATES, 1999-2007. *Mark Canfield, Cara Mai, Ying Wang, Lisa Marengo, Alissa O'Halloran, Richard Olney, Russell Kirby (Birth Defects Epidemiology and Surveillance Branch, Texas Department of State Health Services, Austin TX 78714)

We conducted a population-based epidemiologic study of the relationship between race/ethnicity and 27 major birth defects, using pooled data from 12 US states in the National Birth Defects Prevention Network (NBDPN) that include 13.5 million live births (>1/3 of total US births) over a 9-year period (1999-2007). For both cases and all live births, maternal race/ethnicity was derived from the birth record. Using Poisson regression, prevalence estimates (cases per 10,000 live births, with 95% confidence intervals (CIs)) were calculated for each birth defect and each of 12 racial/ethnic groupings, along with crude and adjusted prevalence ratios (aPRs, with 95% CIs, controlling for maternal age and state of residence), with non-Hispanic whites serving as the referent group. American Indians/Alaska Natives had a significantly higher and 50% or greater prevalence for 7 conditions (e.g. aPR = 4.0 (95% CI = 2.9-5.4) for anotia microtia; aPRs = 1.9-2.1 for cleft lip, lower limb reduction deformities, and encephalocele). Asians (especially Chinese and Asian Indians) had either significantly lower or similar prevalences compared to whites, with the exception of anotia/microtia among Chinese (aPR = 2.1) and Vietnamese (aPR = 1.9) and tetralogy of Fallot among Vietnamese (aPR = 1.6). Among Cubans, we observed 8 significantly lower prevalences (e.g. aPR = 0.4 for trisomy 18). This study represents the first time that there has been sufficient sample size to systematically examine the prevalence of such a range of birth defects across so many racial/ethnic groups, including American Indians, Asian subgroups, and Hispanic subgroups. The relatively high prevalence of selected birth defects in American Indians/Alaska Natives warrants further attention.

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MATERNAL EXPOSURE TO CRITERIA AIR POLLUTANTS DURING EARLY PREGNANCY AND CONGENITAL HEART DEFECTS IN OFFSPRING. *Jeanette A Stingone, Thomas J Luben, Julie L Daniels, Montserrat Fuentes, David B Richardson, Amy H Herring, Arthur S Aylsworth, Marlene Anderka, Lorenzo Botto, Adolfo Correa, Suzanne M Gilboa, Peter H Langlois, Philip J Lupo, Bridget S Mosley, Gary M Shaw, Csaba Siffel, Andrew F Olshan, National Birth Defects Prevention Study (University of North Carolina, Chapel Hill, Chapel Hill NC 27599)

Toxicological and epidemiologic literature indicate that exposure to air pollutants can affect cardiac development. We utilized data from the National Birth Defects Prevention Study, a multisite case-control study, to investigate the relationship between exposure to criteria air pollutants during the critical period of cardiac development, weeks two through eight of pregnancy, and congenital heart defects (CHDs) in offspring. Mothers of cases and controls who conceived between 1997 and 2006 were matched to the closest air monitor using complete residential history. Weekly averages and a seven-week average were constructed for carbon monoxide, nitrogen dioxide, ozone, fine and coarse particulate matter and sulfur dioxide. Sample size ranged from 6120 to 7961, depending upon the pollutant explored. Hierarchical regression models, adjusted for maternal demographics, tobacco and alcohol use, were constructed to address issues of multiple inference when evaluating associations between seven weeks of exposure and both 17 individual CHDs and 6 defect-groupings. Source-factor models were constructed using principal component analysis to assess these relationships in a multipollutant context. Positive associations were observed for several pollutants and CHDs in single and source-factor analyses. Assessing individual weeks of fine particulate matter exposure revealed potential windows of greater susceptibility for selected CHDs, including week 2 for tetralogy of Fallot (odds ratio, OR 1.98 95% confidence interval,CI 1.11,3.46) and week 5 for pulmonary valve stenosis (OR 1.83 95% CI 1.08,3.12) when contrasting women in the highest and lowest deciles of exposure. Several pollutants were shown to increase the odds of CHDs and exploring individual weeks of exposure can reveal potential windows of increased susceptibility during cardiac development. The views expressed are those of the authors and do not necessarily reflect the views or policies of the US EPA.

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VALID GENE-ENVIRONMENT INTERACTIONS WHEN IMPROPER CONTROLS INDUCE SELECTION BIAS. *Ryan Seals, Freya Kamel, Dale Sandler, Howard Hu, Marc Weisskopf (Harvard School of Public Health, Boston MA 02115)

It is widely recognized that the proper selection of controls in case-control studies is one in which the controls represent the distribution of exposure (or exposure person-times) extant in the population giving rise to the cases. In some studies, however, adequate controls may be unavailable, necessitating the use of non-ideal controls. When the exposure distribution of the base population is not faithfully represented by controls, estimates of main effects will generally be biased. Estimates of gene-environment interactions, however, may be unbiased. We provide justification for the estimation of gene-environment interactions in such situations, and demonstrate their validity via simulations. We motivate with a real data example of amyotrophic lateral sclerosis (ALS) and lead exposure. Insufficient numbers of controls were available when the cases had lead levels measured. Additional controls were drawn from a case-control study of Parkinson's disease (PD) in the same population, with approximately ten years between the studies. Temporal trends in lead exposure ensure that an uncorrected main effect for lead will show a spurious association, with controls having lower average lead exposure levels simply due to lower environmental levels. We provide conditions under which gene-environment interactions remain valid in light of such improper control selection. Finally, we explore methods for correcting the main effect estimates by treating the "correct" control exposure levels as missing data, and sensitivity analyses for such corrections.

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MANAGING BIAS IN STUDIES OF ADDITIVE GENE-ENVIRONMENT INTERACTION: GULF WAR ILLNESS. *Robert Haley, Gerald Kramer, Junhui Xiao, Aimee Lam, John Teiber (University of Texas Southwestern Medical Center, Dallas TX 75390)

No prospective records or biomarkers of environmental exposures are available from the 1991 Gulf War. Exposures can only be measured by reports of veterans who know whether they are ill, inviting associations inflated by recall bias. In studying the role of sarin nerve agent in fallout from bombing of Iraqi chemical weapons facilities, we interviewed a representative sample (N = 8,020) of Gulf War veterans, including questions on whether they had been where nerve gas alarms sounded. In a nested case-control subsample (N = 2,095) we determined the PON1 Q192R genotype and measured serum activity of its Q and R isoenzymes. Using Zou's additive interaction calculation, we analyzed the gene-environment interaction of Q isoenzyme activity quartiles and hearing nerve gas alarms with a validated case definition of Gulf War illness. After controlling for multiple possible confounders and for selection bias with a propensity score, we performed a sensitivity analysis to assess the potential effect of recall bias. The crude analysis found a strong interaction on the additive scale with relative excess risk of interaction (RERI) of 7.50 (95% CI 3.84-14.10), attributable proportion (AP) of 0.68 (0.46-0.80), and synergy index (S) of 3.97 (3.02-7.79). Controlling for multiple covariates and the propensity score had modest effect [RERI 5.59 (2.15-12.71), AP 0.62 (0.30-0.78), S 3.350 (1.53-7.38)]. Reclassifying random samples of varying proportions of controls answering No to Yes failed to nullify the interaction until reclassification of >20%. Similarly reclassifying cases answering Yes to No failed until reclassification >20%. Applying both failed until both >10%. Given that a strong gene-environment interaction should not occur with an environmental measurement only due to recall bias and the resistance of this interaction to correction for plausible levels of recall bias, an etiologic role of sarin should not be rejected from concern for bias.

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NOS GENES AND PD: MARGINAL ASSOCIATIONS AND GENE ENVIRONMENT INTERACTIONS WITH PESTICIDES. *Kimberly Paul, Shannon L Rhodes, Janet S Sinsheimer, Myles Cockburn, Jeff M Bronstein, Beate Ritz (University of California, Los Angeles CA 90095)

Background: Nitric oxide (NO) produced by nitric oxide synthase (NOS) enzymes is a potent pro-oxidant that can damage dopaminergic neurons. Thus, the NOS genes are candidates for Parkinson's disease (PD). Organophosphates (OP) are pesticides that induce oxidative stress with widespread agricultural and household use. We investigated the contributions of genetic variation in the NOS genes to PD, assessing interactions between NOS1 and OP pesticides. Methods: In 360 incident PD cases and 816 population controls from Central California, we investigated PD risk with 10 single nucleotide polymorphisms (SNPs), and gene-environment interactions for NOS1 rs2682826 with household OP use and ambient OP exposure estimated via a geographic information system model. Results: Replicating previous findings, we estimated 1.6-2 fold increases in PD risk in variant allele carriers for NOS1 rs1047735 (Odds Ratio (OR) = 1.59, 95% Confidence Interval (CI) = 1.02-2.48), NOS2 rs1060826 (OR = 1.61, 95% CI = 1.05-2.47) and rs2255929 (OR = 1.97, 95% CI = 1.17-3.31), and the interactions between NOS1 rs2682826 and any household pesticide use (OR = 1.75, 95% CI = 0.98-3.12); with stronger interaction effect sizes for household OPs (OR = 2.47, 95% CI = 1.13-5.41). Specifically, there was no effect of the genetic variant for subjects unexposed to household OPs, yet when a subject was exposed to OPs and carried the variant T allele, risk of PD increased 2.6-fold (OR CC + OP = 1.35, 95% CI = 0.77-2.36 vs OR CT/TT + OP = 2.61, 95% CI = 1.45-4.71). We also found risk increases for ambient OP exposure, again the strongest effects were estimated in OP exposed variant T allele carriers (OR CC + OP = 2.09, 95% CI = 1.18-3.71 vs OR CT/TT + OP = 3.35,95% CI = 1.79-6.30). Results did not change when we mutually adjusted for household pesticide use, ambient and occupational exposures to pesticides. Interpretation: Our findings support NOS1 and NOS2 as risk factors for PD and NOS1 rs2682826 as a modifier of OP associations with PD.

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GENETIC VARIANTS IN ONE-CARBON METABOLISM AND DNA REPAIR GENES MODIFY THE ASSOCIATION BETWEEN ARSENIC AND SKIN LESIONS. *Wei Jie Seow, Wen-Chi Pan, Molly Kile, Andrea Baccarelli, Quazi Quamruzzaman, Mahmuder Rahman, Golam Mostofa, Xihong Lin, David Christiani, David Christiani (Harvard School of Public Health, Boston MA 02138)

Background: Single nucleotide polymorphisms (SNPs) can influence susceptibility to arsenic-induced skin lesions. Objective: This study evaluated the association between SNPs from inflammation, one-carbon metabolism and skin cancer pathways and skin lesions. Methods: A case-control study was conducted in Pabna, Bangladesh (2001-2003) and arsenic levels in drinking water were measured. Thirty-eight SNPs were analyzed in 540 cases and 400 controls at the pathway-level using SNP-set Kernel Association Test (SKAT) for their association with skin lesions adjusting for arsenic exposure in drinking water. Logistic regression was then used to estimate the association between each SNP and an interaction term was added to assess gene-environment interactions. Results: Inflammation and one-carbon metabolism pathways were significantly associated with skin lesions (P = 0.03), after adjusting for water arsenic and other covariates. Three SNPs - rs3024496 (IL10, adjusted odds ratio (OR) = 0.68, P = 0.008), rs1832683 (MAT1a, adjusted OR = 1.47, P = 0.03) and rs7946 (PEMT, adjusted OR = 1.42, P = 0.02) - were nominally associated with skin lesions, but did not passed multiple testing correction. Also one-carbon metabolism SNP rs2278952 (PEMT, P for interaction = 0.003) and DNA repair SNP rs2228000 (XPC, P for interaction = 0.005) significantly modified the association between arsenic and skin lesions after adjusting for multiple comparisons. Conclusions: Genetic variants in one-carbon metabolism and DNA repair genes increased susceptibility of arsenic-induced skin lesions.

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GENE-SMOKING INTERACTIONS AND RISK OF CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA AMONG HISPANIC CHILDREN IN A GENOME-WIDE ASSOCIATION STUDY. *Jessica L Trimis, Roberta McKean-Cowdin, W James Gauderman, Anand Chokkalingam, Catherine Metayer, Lisa Barcellos, Yang Wang, Joseph L Wiemels, Patricia A Buffler (University of Southern California, Los Angeles CA 90089)

Background: Findings from recent GWAS suggest that genetic variation may increase a child's risk of acute lymphocytic leukemia (ALL); however, the role of gene-environment interactions is unclear. We use a novel approach to scan the genome for gene-parental smoking interactions. Methods: Participants include self-identified Hispanic subjects from the California Childhood Leukemia Study. Cases (N = 380) were <15 years of age at diagnosis, identified via rapid case ascertainment (<72 hr) at participating California hospitals. Controls (N = 454) were matched to cases on date of birth, gender, and maternal race. Data was evaluated for the presence of multiplicative gene-parental smoking interaction using traditional analytic methods and novel, efficient two step scanning methods implemented using "GxEscan" (http://biostats.usc.edu/software). In each two-step procedure, an initial screening was used to select SNPs for formal GxE testing in step 2. Step 1 tests were based on disease-gene association, environment-gene association or a combination of both. All procedures were constructed to preserve an overall Type I error rate of 0.05. Results: No statistically significant interactions were found with maternal or paternal smoking in all subjects. When we restricted analyses to cases of B-cell ALL (N = 323), one intronic SNP in KCNC3 reached genome-wide significance for maternal smoking in early childhood. Among cases <5 years of age at diagnosis, one SNP reached genome-wide significance for interaction with maternal smoking in early childhood and paternal smoking prior to pregnancy. Ten additional SNPs were identified as potential candidates for replication, but did not reach genome-wide significance. Conclusion: Novel two-step scanning methods can be used in a GWAS to evaluate GxE interactions in studies with relatively small sample sizes while maintaining sufficient power. We are seeking replication in additional studies of childhood ALL to confirm our findings.

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INDOOR COAL SMOKE EXPOSURE, TOBACCO USE, AND LUNG CANCER RISK IN XUANWEI, CHINA. *Christopher Kim, Robert Chapman, Wei Hu, Xingzhou He, H Dean Hosgood, Larry Liu, Hong Lai, Wei Chen, Debra Silverman, Linwei Tian, Bryan Bassig, Min Shen, Yawei Zhang, Shuangge Ma, Nathaniel Rothman, Qing Lan (National Cancer Institute, Rockville MD 20892)

Introduction: Lung cancer rates in Xuanwei County, Yunnan Province are among the highest in China. We have previously reported that indoor combustion of smoky coal for home heating and cooking was associated with increased risk of lung cancer and that this effect varies markedly by coal type. Further, improved stove ventilation is followed by reduction in lung cancer risk. We explored the joint relationship between tobacco use and coal use in Xuanwei men. Methods: We analyzed data from a population-based case–control study of lung cancer in Xuanwei. Cases were identified from four Xuanwei hospitals and controls were selected from the general population by probability sampling. Controls were matched one-to-one with cases on age. In total, 260 cases and 260 controls were analyzed in this study. Tobacco, coal, and solid fuel exposures were tabulated from questionnaires and reported in cigarette pack-years, duration of smoking, and average tons of coal used annually. Odds ratios and 95% confidence intervals were estimated by conditional logistic regression with the main effects of coal, smoking, and coal-smoking interaction terms. Results: Overall, smoking was positively and significantly, although only modestly, associated with lung cancer risk (OR per pack-year: 1.02; 95% CI: 1.01-1.04). The risk of lung cancer per pack-year of smoking decreased as cumulative lifetime use of smoky coal increased (0-50 tons coal: OR: 1.07; 95% CI: 1.01-1.15; >50-150 tons coal: OR: 1.05; 95% CI: 1.01-1.10; >150 tons coal: OR: 1.00; 95% CI: 0.99-1.03; P-interaction: 0.041). Discussion: Our results suggest that the effect of tobacco on lung cancer risk was weaker in men exposed to higher amounts of coal. Results are consistent with previous cohort study findings in Xuanwei. Constituents of coal combustion, such as polycyclic aromatic hydrocarbons, could plausibly act to diminish the carcinogenicity of tobacco through metabolic competition or other possible mechanisms.

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BREAST CANCER RISK PREDICTION WITH HETEROGENEOUS RISK PROFILES ACCORDING TO BREAST CANCER TUMOR MARKERS. *Bernard Rosner, Robert Glynn, Rulla Tamimi, Wendy Chen, Graham Colditz, Walt Willett, Susan Hankinson (Harvard Medical School, Boston MA 02115)

Relationships between some risk factors and breast cancer incidence are known to vary by tumor subtype. However, breast tumors can be classified according to a number of markers, which may be correlated making it difficult with standard competing risk survival analysis to identify heterogeneity of risk factors with specific tumor markers. In this paper, a constrained competing risk survival model is proposed, allowing for assessment of heterogeneity of associations of risk factors according to specific tumor markers while controlling for other markers. These methods are applied to Nurses' Health Study data from 1980 – 2006, Boston, MA, USA, during which 3,398 incident invasive breast cancers occurred over 1.4 million person-years. Results suggest that when ER and PR are mutually considered, some risk factors thought to be characteristic of "estrogen positive tumors" such as high BMI during postmenopause and increased height are significantly associated with ER+/PR+ but not ER+/PR- tumors. This distinction may provide insights into the underlying biology of breast cancer etiology and also appropriate treatment.

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TUMOR MARKERS IN RELATION TO DISEASE-FREE SURVIVAL AMONG WOMEN WITH DUCTAL CARCINOMA IN SITU OF THE BREAST. *Alex Binder, John Hampton, Brian Sprague, Matthew Walsh, Andreas Friedl, Polly Newcomb, Amy Trentham-Dietz (University of Wisconsin-Madison, Madison WI 53726)

Ductal carcinoma in situ (DCIS) constitutes approximately 20% of all new breast cancer diagnoses. As there is no definitive means to determine which cases of DCIS will lead to invasive breast cancer, prognostic markers are needed. To examine the relation between disease-free survival and molecular markers, we prospectively identified new cases of DCIS diagnosed between 1997 and 2000 in Wisconsin women 18-74 years of age from the state cancer registry. Cases completed baseline risk factor interviews about 1 year after initial diagnosis, and provided consent to access medical records and tumor blocks. Tumor markers including Estrogen Receptor (ER), Progesterone Receptor (PR), HER2/neu, Ki-67, and p53 were evaluated using immunohistochemistry. Follow-up interviews gathered information on subsequent breast cancer diagnoses including cancer treatment. Among the 245 DCIS cases, 36 (15%) had a second breast cancer diagnosis (86% confirmed by pathology reports). Median follow-up time through the date of a second breast cancer diagnosis or last interview was 11.2 years (range 0.5-15.0 years). Hazard rate ratios (HR), 95% confidence intervals (CI), and p-values were calculated to compare the occurrence of a second breast cancer diagnosis according to tumor markers using Cox proportional hazards models adjusted for age and treatment. An association was observed between lack of p53 overexpression and a second diagnosis (14% versus 42% for p53-positive versus negative; HR 2.63, 95% CI 1.13, 6.12; $P = 0.02$). Hazard ratios for the other markers were not significant (ER, $P = 0.52$; PR, $P = 0.09$; HER2, $P = 0.64$; Ki-67, $P = 0.20$). These results suggest that the absence of p53 protein in DCIS tumors is a risk factor for a second breast cancer diagnosis. Additional analyses will consider risk factors together with tumor and treatment factors in relation to outcomes after a DCIS diagnosis.

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NOVEL METHODOLOGIES TO ADDRESS MOLECULAR HETEROGENEITY OF DISEASE PROCESSES IN EPIDEMIOLOGIC RESEARCH. *Aya Kuchiba, Molin Wang, Shuji Ogino, Donna Spiegelman (Harvard School of Public Health, Boston MA 02115)

Epidemiologic research typically investigates the associations between exposures and the risk of a disease, in which the disease of interest is treated as a single outcome. However, many human diseases, including colon cancer, type II diabetes mellitus and myocardial infarction, are comprised of a range of heterogeneous molecular and pathologic processes, likely reflecting the influences of diverse exposures. The approach, which incorporates data on the molecular and pathologic features of a disease directly into epidemiologic studies, Molecular Pathological Epidemiology, has been proposed to better identify causal factors and better understand how potential etiologic factors influence disease development. In this study, we present statistical methods for evaluating whether the effect of a potential risk factor varies by subtypes of the disease, in cohort studies, case-control studies and case-case study designs. A new SAS macro is presented, %subtype, to implement these methods. This macro tests overall heterogeneity through the common effect test (i.e., the null hypothesis is that all of the effects of exposure on the different subtypes are the same) as well as pair-wise differences in exposure effects. In adjusting for confounding, the effects are allowed to vary for the different subtypes or they can be assumed to be the same across the different subtypes. To illustrate our methods, we apply %subtype to the study of the effect of alcohol intake on LINE-1 methylation subtypes of colon cancer in the Health Professionals Follow-up Study, where 51,529 men have been followed since 1986 during which time 268 cases of colon cancer have occurred. Results are presented for all 3 possible study designs for comparison purposes.

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BREAST CANCER SUBTYPES AND PREVIOUSLY ESTABLISHED GENETIC RISK FACTORS: A BAYESIAN APPROACH. *Katie O'Brien, Stephen Cole, Lawrence Engel, Jeannette Bensen, Charles Poole, Amy Herring, Robert Millikan (UNC-Chapel Hill, Chapel Hill NC 27599)

Gene expression analyses indicate that breast cancer is a heterogeneous disease with at least 5 immunohistologic subtypes. Despite growing evidence that these subtypes are etiologically and prognostically distinct, few studies have investigated whether they have divergent genetic risk factors. To help fill in this gap in our understanding, we examined associations between breast cancer subtypes and previously established susceptibility loci among white and African-American women in the Carolina Breast Cancer Study. We used Bayesian polytomous logistic regression to estimate odds ratios (ORs) and 95% posterior intervals (PIs) for the association between each of 78 single nucleotide polymorphisms (SNPs) and 5 breast cancer subtypes. Subtypes were defined using 5 immunohistochemical markers: estrogen receptors (ER), progesterone receptors (PR), human epidermal growth factor receptors 1 and 2 (HER1/2) and cytokeratin (CK) 5/6. Several SNPs in TNRC9/TOX3 were associated with luminal A (ER/PR+, HER2-) or basal-like breast cancer (ER-, PR-, HER2-, HER1 or CK 5/6+), and one SNP (rs3104746) was associated with both. SNPs in FGFR2 were associated with luminal A, luminal B (ER/PR+, HER2+), or HER2+/ER-disease, but none were associated with basal-like disease. We also observed subtype differences in the effects of SNPs in 2q35, 4p, TLR1, MAP3K1, ESR1, CDKN2A/B, ANKRD16, and ZM1Z1. We found evidence that genetic risk factors for breast cancer vary by subtype and further clarified the role of several key susceptibility genes.

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CHANGE OF MAMMOGRAPHIC DENSITY PREDICTS THE RISK OF CONTRALATERAL BREAST CANCER. *Maria EC Sandberg, Jingmei Li, Per Hall, Mikael Hartman, Isabel dos-Santos-Silva, Keith Humphreys, Kamila Czene (Karolinska Institutet, Stockholm Sweden)

Introduction: Mammographic density is a strong risk factor for breast cancer, but it is unknown whether density at first breast cancer diagnosis and changes during follow-up influences risk of non- simultaneous contralateral breast cancer (CBC). Methods: We collected mammograms for CBC-patients (cases) and unilateral breast cancer patients (controls), individually matched on age and calendar period of first breast cancer diagnosis, type of adjuvant therapy and length of follow-up. The odds of CBC as a function of changes of density during follow-up were investigated using conditional logistic regression, adjusting for non-dense area at diagnosis. Results: Patients who experienced $\geq$10% absolute decrease in percent density had a 55% decreased odds of CBC (Odds Ratio (OR) = 0.45 95% CI: 0.24-0.84) relative to patients who had little or no change in density from baseline to first follow-up mammogram (mean = 1.6 (standard deviation = 0.6) years after diagnosis), whereas among those who experienced an absolute increase in percent density there was little change in the odds of CBC (OR = 0.83 95% CI: 0.24-2.87). Conclusion: Decrease of mammographic density within the first two years after a first diagnosis is associated with a significantly reduced risk of CBC. This potential new risk predictor can thus contribute to decision making as well as provide reassurance to the patients at decreased risk.

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A PROSPECTIVE STUDY OF SMOKING IN RELATION TO BREAST CANCER INCIDENCE IN AFRICAN AMERICAN WOMEN.

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Many studies have found that women with substantial pack-years of active smoking are at increased risk of breast cancer, and some evidence suggests that passive smoking (exposure to the smoke of others) increases the risk of premenopausal breast cancer. Evidence about smoking and breast cancer specifically in African Americans is sparse. We carried out a prospective study of smoking and breast cancer incidence in African American women, based on 1,377 incident cases of invasive breast cancer identified from 1995 to 2009 during 14 years of follow-up in the Black Women's Health Study. Incidence rate ratios (IRR) and 95% confidence intervals (CI) for categories of active and passive smoking, relative to no active or passive smoking, were calculated from Cox proportional hazards models, controlling for breast cancer risk factors. Active smoking was associated with increased risk of premenopausal breast cancer: the IRR for beginning smoking before age 18 together with accumulation of ≥20 pack years was 1.70 (95% CI 1.05-2.75). IRRs did not vary appreciably according to whether active smoking began before or after the first birth. The positive associations of active smoking with premenopausal breast cancer were most apparent among women with a body mass index <25kg/m2 and for estrogen receptor positive cancer. Based on limited information on passive smoking at home and work through age 30, the IRR associated with exposure to passive smoking only was increased for premenopausal breast cancer, IRR = 1.42 (95% CI 1.09-1.85). These results add to the evidence that exposure to tobacco smoke increases the risk of breast cancer.

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DIABETES, INSULIN USE AND OVARIAN CANCER INCIDENCE.

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Previous studies support an association between type II diabetes and increased risk of several cancers, including breast, endometrial, colorectal, liver and pancreatic cancer. However, the evidence for an association with ovarian cancer is unclear, and few large prospective studies of this association are available. We examined associations of self-reported, physician-diagnosed diabetes and use of insulin or oral hypoglycemic medications with incidence of epithelial ovarian cancer among 110,493 women in the Nurses' Health Study. Data on diabetes diagnoses were collected every two years beginning in 1976, and use of insulin and oral hypoglycemic agents was assessed in 1988 and every two years from 1994-2008. We used age- and multivariable-adjusted Cox proportional hazards regression to estimate incidence rate ratios (RR) and 95% confidence intervals (CI). Between 1976 and 2010, 1,015 incident cases of ovarian cancer were diagnosed, including 55 cancers in women with diabetes. In analyses adjusted for age, oral contraceptive use, parity, menopausal status, postmenopausal hormone use and body mass index (BMI), there was no evidence of an association between history of diabetes and incidence of ovarian cancer (RR = 1.01; 95% CI = 0.76-1.33). The results were unchanged when BMI was excluded from the model. In analyses that considered the duration of diabetes, there was no clear association among women with >5 (RR = 1.13; 95% CI = 0.82-1.58) or >10 (RR = 1.29; 95% CI = 0.88-1.91) years since diabetes diagnosis. Among diabetic women, there was no evidence of an association between use of insulin (RR = 0.76; 95% CI = 0.32-1.77) or oral hypoglycemic medications (RR = 0.90; 95% CI = 0.47-1.75) and ovarian cancer incidence, although these analyses had limited power. Our results indicate that type II diabetes and medications commonly used by diabetic individuals do not increase the risk of epithelial ovarian cancer.

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ADOLESCENT AND ADULT DIETARY FAT INTAKE AND OVARIAN CANCER RISK.

*Megan Rice, Shelley Tworoger (Brigham and Women's Hospital, Boston MA 02115)

Purpose: Ovarian cancer is the 5th leading cause of cancer death for women in the US, however prevention recommendations have been limited because few confirmed risk factors are modifiable. While dietary fat has been proposed as a potential risk factor, results have been inconsistent possibly due to limitations of when diet was assessed (e.g., baseline only) preventing the investigation of diet at different periods in life or changes over time. Therefore, we examined the association between dietary fat intake in adolescence and adulthood and risk of ovarian cancer in a large prospective cohort study. Methods: We assessed cumulative average adult dietary fat intake, including total, animal, vegetable, saturated, and unsaturated fat, among 78,174 women in the Nurses' Health Study (NHS) using food frequency questionnaires administered every 4 years beginning in 1980. NHS participants also provided information on dietary fat intake in adolescence in 1986. Between 1980 and 2008, we identified 468 cases of ovarian cancer. We used Cox proportional hazards regression to estimate the association between adolescent and adult dietary fat intake and risk of ovarian cancer. Results: There were no significant associations between any of the measures of adolescent dietary fat intake and risk of ovarian cancer. Similarly, there were no significant associations between adult dietary fat intakes and risk of ovarian cancer among women in the NHS. While women in the highest quintile of adult total fat intake had 23 percent higher risk of ovarian cancer compared to those in the lowest quintile, this association did not reach statistical significance (95% CI: 0.90, 1.67, p-trend = 0.15). Conclusion: There was no significant association between adolescent or adult dietary fat intake and risk of ovarian cancer in the NHS. Future work will incorporate the NHSII as well as assess whether these associations vary by histological subtype or participant characteristics.

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THE ASSOCIATION BETWEEN COLORECTAL CANCER SUSCEPTIBILITY LOCI AND COLORECTAL CONVENTIONAL ADENOMAS AND SERRATED POLYPS.

*Andrea Burnett-Hartman, Polly Newcomb, Carolyn Hutter, Ulrike Peters, Lee-Ching Zhu, Melissa Upton, Karen Makar (Fred Hutchinson Cancer Research Center, Seattle WA 98109)

Genome wide association studies (GWAS) of colorectal cancer (CRC) have identified consistently replicated CRC susceptibility loci. However, the relationship between these loci and different types of colorectal polyps is not well-established. We conducted a case-control study of the association between GWAS-identified CRC susceptibility loci and subsets of colorectal polyps, including conventional adenomas and serrated polyps. Participants were enrollees of Group Health, ages 24-79, who self-reported as White, received a colonoscopy from 1998-2007, donated a buccal cell or blood sample, and completed a structured questionnaire. Polyps underwent a standard pathology review. We used the Illumina GoldenGate assay to perform multiplex genotyping of 13 GWAS-identified CRC susceptibility single nucleotide polymorphisms (SNPs) that had $P < 5 \times 10 - 7$ based on prior GWAS. Polytomous logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between subsets of polyps and the GWAS-identified CRC risk alleles for each SNP under a log-additive model. Analyses included 679 controls, 418 conventional adenoma cases, and 356 serrated polyp cases. Comparing polyp cases to controls, we observed statistically significant ($P < 0.05$) associations between conventional adenomas and the CRC risk allele for: *MYNN*/3q26.2 (rs10936599, OR = 1.24; 95% CI: 1.01-1.51), *CDH1*/16q22.1 (rs9929218, OR = 1.24; 95% CI: 1.02-1.51), and 20p12.3 (rs961253, OR = 1.23; 95% CI: 1.03-1.48). For serrated polyps, only 20p12.3 (rs961253, OR = 1.24; 95% CI: 1.02-1.50) was statistically significant. Among these SNPs, only the associations with the CRC risk allele at *CDH1*/16q22.1 were statistically significantly different between conventional adenomas and serrated polyps ($P = 0.02$). These results may help elucidate pathway-specific mechanisms for CRC initiation and inform investigations into the function of GWAS-identified CRC susceptibility loci.

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OVARIAN CANCER RISK FACTORS BY TUMOR SIDE.

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Background: The left ovary is endowed with more germ cells at birth than the right and endometriosis tends to occur more on the left, while the right ovary is contiguous to the appendix. These differences in embryologic development and pelvic symmetry could lead to varying ovarian cancer laterality by histologic type. Methods: Tumor measurements were abstracted from pathology reports on 1638 epithelial ovarian cancer cases participating in the New England Case Control study. 61 cases (3%) and 97 controls (5%) with prior unilateral oophorectomy for benign disease (34% right, 32% left, 35% unknown side) were excluded as well as cases with no dominant side (n = 593) or missing side (n = 5). We used polytomous logistic regression to calculate odds ratios (OR) and 95% confidence intervals (CI). Results: We observed a similar number of left and right sided tumors for both unilateral (391 vs. 387) or dominant (517 vs 519) cases, and no statistically significant difference in laterality by histologic subtype. In particular, endometrioid and clear cell tumors were not more frequent or dominant on the left nor mucinous tumors more frequent or dominant on the right. The risk for left- or right-sided tumors did not differ for most ovarian cancer risk factors, including oral contraceptive use, parity, endometriosis, and family history of ovarian cancer. However, tubal ligation was less common among cases with right-sided tumors (9%) than cases with left-sided tumors (14%) translating into lower risk for right-sided tumors (OR = 0.56, 95% CI = 0.40-0.77) than left-sided tumors (OR = 0.86, 95% CI = 0.65-1.14; p-het = 0.03). The difference was most striking among mucinous tumors with 18% of women with left sided tumors reporting a tubal ligation but only 3% with right-sided tumors (p = 0.001). Conclusion: These data suggest that most risk factors do not influence the side of ovarian tumor development, but tubal ligation may influence the location of mucinous tumor growth.

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CHRYSOTILE ASBESTOS EXPOSURE AND OVARIAN CANCER: IS THERE AN ASSOCIATION?

*Megan Jacobsen, Amina Foda, Christopher Ronk, Meg McKinley (ChemRisk LLC, San Francisco CA 94105)

The IARC recently concluded that sufficient evidence exists to support a causative association between all commercial forms of asbestos and ovarian cancer. Published toxicology and epidemiology studies have reported cancer potency differences for the various asbestos fiber types. For example, several recent analyses have suggested that chrysotile exposures have minimal, if any, potency for causing mesothelioma. We performed a systematic review of the epidemiology literature to evaluate the possible association between asbestos-exposed subjects and ovarian cancer as a function of fiber type. Over 30 studies were evaluated. Eight studies reported relative risk estimates (RR) for ovarian cancer in subjects exposed primarily to chrysotile asbestos, ranging from 0.67 to 7.69. A meta-RR for the association between chrysotile exposure and ovarian cancer was not statistically significant at 2.4 (95% CI: 0.4, 13.9). Likewise, the meta-RR was also not statistically significant for amphibole exposed subjects (1.6; 95% CI: 0.6, 4.8), based on only two studies. For mixed exposure, a significantly increased meta-RR of 2.2 (95% CI: 1.3, 3.8) was observed, based on five studies. Our findings indicate a possible association between ovarian cancer and exposure to mixed asbestos fibers, but not chrysotile alone. These results support a difference in carcinogenicity between fiber types and also suggest that there may be one or more different biological mechanisms of carcinogenesis for asbestos in the ovary, compared to other organ systems.

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DIETARY PATTERNS AND RISK OF HODGKIN LYMPHOMA IN A POPULATION-BASED CASE-CONTROL STUDY.

Brenda Birmann, *Mara Epstein, Ellen Chang, Yawei Zhang, Teresa Fung, Julie Kasperzyk, Richard Ambinder, Tongzhang Zheng, Nancy Mueller (Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School; Department of Epidemiology, Harvard School of Public H, Boston MA 02115)

Over 9,000 new cases of Hodgkin lymphoma (HL) are diagnosed in the US each year. Etiologic factors for HL include social and other predictors of delayed childhood infection. The role of diet in HL etiology is unclear, and no study to date has evaluated dietary pattern in association with HL risk. We analyzed 482 cases of classical HL (cHL) and 635 population-based controls from Massachusetts and Connecticut who completed a baseline interview and a 61-item food frequency questionnaire in 1997-2000. We used principal components analysis to identify four major diet patterns (High vegetable, Western, fruit/low-fat dairy, and desserts/sweets, in order of eigenvalues). We used multivariable logistic regression to compute odds ratios (OR) and 95% confidence intervals (CI) for the association of quartile of diet pattern score with cHL risk, adjusting for age, gender, state, total calories and body mass index in all subjects and in strata defined by age (<50 vs. ≥50 years) and gender. A desserts/sweets diet was positively associated with risk of younger-adult (age <50 years; case/control N = 310/411; OR(Q4 vs. Q1): 1.96, 95% CI: 1.26, 3.03, p_{trend} = 0.0007), but not older-adult cHL (age ≥50 years; case/control N = 63/97; p_{trend} = 0.60). The Western diet pattern had a suggestive positive association with risk of older-adult (OR(Q4 vs. Q1): 2.75, 95% CI: 0.84, 8.94, p_{trend} = 0.07) but not younger-adult cHL (p_{trend} = 0.89). A high vegetable diet was associated with a lower risk of cHL at all ages (OR(Q4 vs. Q1): 0.64, 95% CI: 0.43-0.97, p_{trend} = 0.05). The fruit/low-fat dairy pattern was not associated with cHL risk, and results did not differ notably by gender. Analyses by histologic subtype and tumor Epstein-Barr virus status are ongoing. Our preliminary results provide the first evidence for a role of diet pattern in cHL etiology. Specifically, a diet high in desserts and sweets may increase cHL risk, whereas a vegetable-rich diet may reduce risk.

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VARIATIONS WITHIN ARID5B, CEBPE, AND IKZF1 AND RISK OF CHILDHOOD LEUKEMIA.

*Ling-I HSU, Anand Chokkalingam, Catherine Metayer, Joseph Wiemels, Lisa Barcellos, Patricia Buffler (University of California, Berkeley, CA 94704)

Leukemia is the most common childhood malignancy, accounting for 31% of all cancers diagnosed in children younger than 15 years old. Two genome-wide association studies found that genes involved in B-lymphocyte development, including IKZF1 (7p12.2), ARID5B (10q21.2),and CEBPE (14q11.2) are associated with ALL predisposition among the Caucasian population. Here, we attempted to validate selected single nucleotide polymorphisms (SNPs) from previous GWAS in Hispanic population in the California Childhood Leukemia Study (CCLS). In addition, potential gene and environment interactions between candidate genes and early life infection experiences (early daycare attendance) were assessed. The study population is comprised of 323 Hispanic ALL cases and 454 controls from the CCLS. We examined the associations between these three genes identified in previous GWAS and childhood ALL risk and gene environment interactions. Logistic regression assuming a log-additive genetic model of inheritance was used to estimate odds ratios(OR) associated for each SNP, adjusting for age, sex, principal components. In the Hispanic population, results for SNPs in ARID5B, CEBPE, and IKZF1 were consistent with previous GWAS findings after accounting for multiple testing. We also examined the associations within ALL subtypes. ARID5B SNPs showed stronger association with ALL when the analysis was confined to B-cell ALL and B-cell yperdiploidy ALL. The results from our study confirm that previous GWAS-identified SNPs in B-cell development genes are associated with childhood ALL risk in the Hispanic population and might lead to leukemogenesis. Further investigations are needed to both fine-map the gene regions for identification of the causal loci, and to identify environment factors that may modulate the effects of these loci.

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ASSOCIATIONS BETWEEN ENDOGENOUS HORMONE LEVELS AND LOBULAR INVOLUTION IN THE NORMAL BREAST AMONG PREMENOPAUSAL WOMEN. *Zeina Khodr, Mark Sherman, Ruth Pfeiffer, Gretchen Gierach, Louise Brinton, Roni Falk, Deesha Patel, Daniel Visscher, Carolyn Mies, Stephen Hewitt, Susan Clare, Anna Maria Storniolo, Jonine Figueroa (National Cancer Institute, Rockville MD 20852)

Background: Terminal duct lobular units (TDLUs) are the structures from which most breast cancers arise. TDLU involution (i.e., atrophy and loss of TDLUs) has been related to reduced breast cancer risk. Hormones may influence TDLU involution; therefore, we assessed this relationship in normal breast tissues from women in the Komen Tissue Bank (KTB). Methods: Subjects included premenopausal women (n = 422) who donated breast tissues for research in the KTB (2009-2011). A pathologist, masked to patient data, determined TDLU number, diameter, and number of acini (epithelial substructures within TDLUs) for up to ten TDLUs from one breast tissue section per woman. Serum levels of estradiol (E2), sex hormone-binding globulin (SHBG), follicle-stimulating hormone, prolactin, testosterone, and progesterone were measured. Ordinal logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for associations of TDLU numbers, median TDLU diameter, and median acini count with hormone levels in tertiles (T). Models were stratified by oral contraceptive (OC) use, yes (n = 174) and no (n = 248), and adjusted for age, body mass index, parity, and menstrual cycle phase (non-OC users only). Results: Among OC users, higher prolactin levels were significantly associated with higher TDLU numbers (ORT3 vs. T1: 3.30, 95% CI: 1.62-6.75; p-trend = 0.001). Similar trends were seen between prolactin and acini count among OC users (p-trend = 0.2053) and non-OC users (p-trend = 0.0663), although they were not statistically significant. There were no significant trends between all other hormone levels with TDLU measurements. Conclusion: Higher prolactin levels, which have been associated with increased breast cancer risk, were related to decreased TDLU involution in normal breast tissues of premenopausal OC users. Future research of hormonal influences on TDLU involution, a potential intermediate marker of breast cancer risk, in other studies is needed.

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RECRUITING FEMALE CANCER SURVIVORS FROM THE GEORGIA CANCER REGISTRY: THE FUCHSIA WOMEN'S RESEARCH STUDY. *Penelope P Howards, Konny H Kim, Jill J Woodard, Siyu Zhang, Pamela J Mink, Kevin C Ward (Emory University, Atlanta GA 30322)

With improved survival after cancer diagnosis, the need to study the long-term health and quality-of-life of cancer survivors has increased. However, population-based recruitment of cancer survivors is challenging. The FUCHSIA Women's Study is a study of fertility in female survivors of young adult cancers recruited from the Georgia Cancer Registry (GCR), a statewide population-based registry. Eligibility criteria included being alive, female, aged 20-35 at diagnosis, diagnosed between 1990-2009 in metropolitan Atlanta or 1995-2009 in the rest of Georgia, at least 2 years post-diagnosis, and between the ages of 22-45 currently. All invasive cancers and in situ breast cancers were eligible for inclusion except non-melanoma skin cancer. The GCR included 5,424 women meeting these criteria; 61% of whom were contacted successfully by mail or phone. Of those, 484 refused further contact, 54 were ineligible, and 193 neither agreed nor refused. Of the 2,580 women who agreed to be contacted by the study, 49% completed the interview, 8% were no longer eligible, 15% refused, and 28% were unable to be reached. The age distribution of the women who completed the interview was similar to the age distribution for all eligible women, but participation varied across cancer diagnosis from 15% for cancer of the cervix uteri to 28% for breast cancer. Of the eligible women, white women were more likely to complete the interview (25% of all eligible) compared with African American women (19% of all eligible). The greatest challenge to recruiting women in the GCR was being able to contact them, which was affected by incorrect contact information, call screening, and busy schedules of eligible women. When reached, survivors were more likely to participate than to refuse.

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INTERACTION OF COFFEE INTAKE AND BODY MASS INDEX ON THE RISK OF ADVANCED BREAST CANCER AMONG SINGAPORE CHINESE WOMEN. *Lei Zhu, Lesley M Butler, Renwei Wang, Woon-Puay Koh, Mimi C Yu, Jian-Min Yuan (Colorado State University, Fort Collins CO 80523)

Background: Experimental data support both a protective and risk enhancing effect of various coffee-related compounds on breast cancer development. Although prospective epidemiologic data do not support a relationship between coffee intake and breast cancer risk overall, women with larger body size may be more susceptible to the effects of coffee on breast cancer risk. Objective: Using data from a prospective cohort of Singapore Chinese women, we examined the relation between coffee intake and breast cancer risk. Methods: At baseline, between 1993 and 1998, we collected information on dietary history from 35,303 Singapore Chinese women aged 45 to 74 years. Using Cox regression models, we calculated hazard ratios (HRs) and 95% confidence intervals(CIs) adjusted for potential confounders. Stratified analysis by BMI was conducted to evaluate potential effect modification. Results: After a mean follow-up of 11 years, 629 women developed breast cancer. Average intake among coffe drinkers was 1.5 cups/day (interquartile range = 0.8, 2.3). Coffee intake more than 2 cups/day was weakly associated with increased breast cancer risk, compared with none or monthly intake. The positive association strengthened and became statistically significant for risk of advance breast cancer (HR = 1.90; 95% CI: 1.30, 2.77; $P_{trend} < 0.01$). In stratified analyses, the adverse effect of coffee intake on the development of advanced breast cancer was present only among larger women (BMI>median, 23 kg/m2) (HR = 2.35; 95% CI: 1.51, 3.66; comparing daily intake versus none; P for interaction = 0.02). Conclusion: We provide novel prospective findings for an adverse effect of coffee on the advanced breast cancer risk among Chinese women. Our data suggest that a higher BMI may influence the adverse effect of coffee on advanced breast cancer development. Keywords: Advanced disease, Body mass index, Breast cancer, Coffee

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DOSE-RESPONSE RELATIONSHIP BETWEEN PAAN CHEWING AND ORAL CANCER. *Sreenath Madathil, Marie Claude Rousseau, Paul Allison, Willy Wynant, Gopalakrishnan Netuveli, Ipe Varghese, Shameena Shiraz, Genevieve Castonguay, Akhil Soman, Shahul Hameed, Belinda Nicolau (McGill University, Montreal QC Canada)

The association between paan-chewing habit (PCH) and oral cancer risk is well documented. However, few studies have investigated the dose-response relationship between them, and all of these studies adopted trend analysis. Spline models offer an alternative that circumvents the forced assumption of linearity and power loss associated with categorization of exposure. Objectives: To estimate the dose-response relationship between PCH and oral cancer risk, for duration and average lifetime frequency of PCH. Methods: In a hospital-based case-control study, the HeNCe Life study-India, incident cases (N = 350) of oral squamous cell carcinoma (OSCC) were recruited from 2 major public hospitals in Kozhikode, India. Non-cancer controls (N = 371), frequency matched by age and sex, were recruited from different outpatient clinics of the same hospitals. Data on socio-demographic and behavioral factors were collected using a questionnaire and a life-grid technique. The average lifetime frequency of PCH was measured as number of paan quids chewed per day and duration was measured in years. We used descriptive statistics and restricted cubic logistic regression spline to test dose-response relationships. Results: The majority of the OSCC cases had PCH (72%) while only 18% of the controls had the habit. Contrary to previous studies, a nonlinear dose-response was observed between average frequency and duration of PCH, and risk of OSCC among males and females. There was no further increase in risk observed for an average frequency above 7 & 8.5 quids/day and duration above 60 & 35 yrs for females and males,respectively. Conclusion: We observed a nonlinear dose-response relationship between PCH and oral cancer. The results may have implications for the development of gender specific, individualized risk assessment and effective paan cessation programs.

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PARTICIPATION BIAS IN A PROSTATE CANCER QUALITY OF LIFE SURVEY. Brian Kim, *Kimberly Porter, Richard Contreras, Anil Thomas, Jeff Slezak, Steven Jacobsen, Gary Chien (Kaiser Permanente, Pasadena CA 91101)

Introduction and Objective: Patient surveys are a valuable tool for measuring the impact of a disease or treatment. Surveys may be marred however, by poor participation rates potentially introducing bias if participants differ from non-participants in important characteristics. The study objective was to identify potential demographic and clinical factors associated with participation in a prostate cancer quality of life survey. Methods: From March 2011 to September 2012, men with biopsy-proven prostate cancer were asked to participate in a quality of life study at 12 Kaiser Permanente, Southern California hospitals. Men completed the Expanded Prostate Cancer Index Composite (EPIC-26) at the time of their prostate biopsy and at follow-up intervals after initiating treatment (1, 3, 6, 12, 18, and 24 months). Surveys were administered in English or Spanish. Select demographic and clinical parameters were compared between participants (those that completed a baseline and any follow-up survey) and non-participants (those that completed only a baseline survey) using chi-squared and ANOVA tests. Results: A total of 1698 men were enrolled in the study (1073 participants; 625 non-participants; participation rate = 63.2%). Men who participated tended to be older (OR = 2.5; 1.5-4.2), partnered (OR = 1.9; 1.4-2.5), English-speaking (OR = 1.5; 0.8-3.2), Caucasian (OR = 1.2; 0.9-1.7), and living in areas with higher education ($p = 0.01$) and income levels ($p = 0.001$). Men with a family history for prostate cancer were also more likely to participate (OR = 1.4; 1.0-1.8). PSA levels, biopsy Gleason sum, Charlson co-morbidity index, BMI, and smoking status were similar amongst all men. Conclusions: These data suggest that the survey results will have to be interpreted in light of these demographic differences, as they may be associated with quality of life. Moreover, this information can be used for targeted retention efforts in this and other prostate cancer quality of life studies.

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HUMAN PAPILLOMAVIRUS VACCINE BELIEFS, ACCEPTANCE, AND UPTAKE AMONG U.S. AND INTERNATIONAL STUDENTS AT A MID-WESTERN UNIVERSITY. *Madhav Bhatta, Sameer Gopalani (College of Public Health Kent State University, Kent OH 44242)

Globally cervical cancer is a major health issue among women. Despite the availability of two human papillomavirus (HPV) vaccines for prevention of cervical cancer, increasing the vaccination rates remains a global challenge. This study assessed beliefs, acceptance and uptake of HPV vaccines among U.S. (citizen/permanent resident) and international students at a Mid-Western University. A cross-sectional study conducted among a random sample of 502 students using an anonymous self-administered online and paper-based survey that assessed socio-demographics, HPV vaccine knowledge, beliefs, acceptance, and uptake. Logistic regression models assessed the relationship between student characteristics and HPV vaccine beliefs, acceptance and uptake. Of 502 participants, 27.7% were international students primarily from Asia; 24.2% were male; 82.8% were single; and the median age was 23.0 years. International students were significantly less likely to agree that males and females of recommended age should be vaccinated [Odds Ratio (95% Confidence interval): 0.61 (0.40, 0.92)]. Overall, 5.5% had any moral or religious reasons against vaccinating and 5.5% had a negative view of HPV vaccines, with no significant difference between the two groups. International students were less likely to perceive HPV vaccines as safe [0.38 (0.25, 0.59)]. Overall, 39.4% and 5.8% U.S. and international students respectively reported receiving at least one dose of HPV vaccine. Female [24.6 (7.5, 80.9)], single [4.0 (1.8, 8.8)], and U.S. [6.9 (3.1, 15.4)] students were more likely to have received at least a single dose of HPV vaccine. However, international students expressed a higher likelihood of receiving HPV vaccine in the future (30.9% vs. 14.9%; $p < 0.001$) than the U.S. students. The low HPV vaccine uptake rates among these international students, who most likely are to be from the higher socioeconomic strata, suggest even lower uptake rates in their home country populations.

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REPRODUCTIVE AND HORMONAL FACTORS, BENIGN BREAST AND REPRODUCTIVE CONDITIONS, AND THYROID CANCER RISK. *Melissa Braganza, Amy Berrington de González, Alina V Brenner, Cari M Kitahara (Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda MD 20892)

Background: Thyroid cancer incidence is notably higher in women compared to men, suggesting that sex hormones may play a role in thyroid cancer etiology; however, results from observational studies on reproductive and hormonal factors have been inconsistent. The few studies examining benign breast and reproductive conditions in relation to thyroid cancer risk have reported positive associations between personal history of benign breast or endometriosis and risk of thyroid cancer. Methods: Using data from the Prostate, Lung, Colorectal, Ovarian (PLCO) Cancer Screening Trial, a prospective cohort with 73,048 U.S. women, between the ages of 50 and 78 years, we calculated hazard ratios (HRs) and 95% confidence intervals (CIs) for self-reported reproductive and hormonal history and personal history of benign breast disease, benign ovarian tumors/cysts, endometriosis, and uterine fibroids in proportional hazards models with age as the time metric and adjusting for education, race/ethnicity, marital status, family history of thyroid cancer, body mass index, and cigarette smoking status. Results: During a median of 11 years of follow-up, 127 women were diagnosed with first primary thyroid cancer (median age = 67 years). Older age at menarche was associated with a reduced risk of thyroid cancer (≥14 vs. <12 years: HR = 0.62, 95% CI: 0.36-1.05). Among parous women, thyroid cancer risk decreased with increasing age at first birth. Older age at natural menopause was associated with a two-fold increased risk of thyroid cancer (≥55 vs. 50-54 years: HR = 2.08, 95% CI: 1.18-3.65). No clear associations were observed for oral contraceptive use or hormone therapy use. Personal history of benign ovarian tumors/cysts (HR = 1.50, 95% CI: 0.95-2.39) or uterine fibroids (HR = 1.72, 95% CI: 1.18-2.50), but not benign breast disease or endometriosis, was associated with an increased risk of thyroid cancer. Conclusion: Results of this prospective study support a possible role of sex hormones in thyroid cancer development.

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MODE OF COLON CANCER DETECTION AND STAGE AT DIAGNOSIS: INTERACTIONS WITH AGE AT DIAGNOSIS AND IMPLICATIONS FOR SCREENING. *Garth Rauscher, Katherine Brewer, Jennifer Parsons, Elizabeth Calhoun, Carol Ferrans (University of Illinois at Chicago, School of Public Health, Division of Epidemiology and Biostatistics, Chicago IL 60612)

Purpose: Colon cancer screening reduces stage at diagnosis and related treatment morbidity. We examined associations of age at diagnosis and mode of detection with stage at diagnosis in the ongoing Colon Cancer Patterns of Care in Chicago study. Methods: Newly diagnosed men and women were ascertained at 7 facilities in metropolitan Chicago, Illinois (two public, two private non-academic, and three academic institutions). Patients were eligible if they were diagnosed with a first primary invasive colon cancer between the ages of 30 and 79, and were non-Hispanic (nH) White or nH Black (response rate = 55%, N = 168 patients). Screen-detection (SD) was defined as discovery through a routine procedure not prompted by symptoms (vs. symptomatic detection). Stage at diagnosis was available on 108 patients. Two binary variables for stage at diagnosis were defined. Early (small and localized) stage was defined as stage 1 (vs. stage 2,3,4). Late (non-localized) stage was defined as stage 3,4 (vs. stage 1,2). Logistic regression models of stage included terms for age, race, and mode of detection and their products, and marginal standardization was used to estimate average percentage point differences (PPD) in risk of early and late stage diagnosis. Results: As expected, SD was associated with increased early stage disease (PPD = 34, $p < 0.06$) and decreased late stage disease (PPD = -16, $p = 0.10$). Despite screening, however, 4 in 10 SD patients were still diagnosed with late stage disease (40%, 95% CI: 20%, 53%). The relation between age and stage varied by mode of detection: for symptomatic patients, risk of late stage dropped precipitously with age, whereas for SD patients, risk of late stage increased with age. Conclusion: Patients should be screened at the earliest possible age consistent with guidelines in order to minimize the diagnosis of late stage tumors and maximize the value of screen detection.

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RADON AND LUNG CANCER. PRELIMINARY RESULTS OF A COHORT STUDY IN A SPANISH RADON PRONE AREA.

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Residential radon is the second cause of lung cancer after tobacco and the first in never smokers. Available evidence comes mainly from case-control studies which have shown, in general, higher residential radon concentrations in cases' dwellings compared with controls. A pilot cohort study with a median follow-up of 12 years after radon measurement showed a risk of 6,6 (95% CI 1,2-38) for lung cancer mortality for those exposed to radon concentrations higher than 148Bq/m3, though only 211 individuals were included (Ruano-Ravina et al. Epidemiology. 2009. 20 (1): 155-6). The aim of this research is to replicate these results in the same population. We designed a cohort study where participants were recruited from the Galician census through a stratified random sampling. Radon measurements took place between 2002 and 2006. Individuals with radon measurements after 2006, individuals younger than 30 at radon measurement and those who had lived for less than 10 years in the same dwelling were excluded. We assessed the vital status of participants through the Galician Mortality Registry and checked which participants had a lung cancer death since radon measurement until 31 December 2011. Results were analyzed with logistic regression where the independent variable is radon concentration (categorized as: below or above 148Bq/m3). 844 individuals took part in the cohort and 21 developed lung cancer during the follow-up. Median follow-up since radon measurement was 8,6 years. Median radon concentration of lung cancer cases was 86 Bq/m3 while for those who did not develop lung cancer was 66 Bq/m3. Cases lived at the same home for a longer time than controls. The adjusted Odds Ratio for lung cancer was 1,35 (95% CI 0,44-4,18) for individuals exposed to residential radon concentrations above 148Bq/m3. In this cohort study radon seems to have no effect on lung cancer though the risk of bias due to a short follow-up period cannot be disregarded.

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RESIDENTIAL RADON AND LUNG CANCER IN NEVER SMOKERS. PRELIMINARY RESULTS OF THE LUNG CANCER RISK FACTORS IN NEVER SMOKERS (LCRINS) STUDY.

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Residential radon is the second cause of lung cancer after smoking. There are very few studies that have analyzed radon and lung cancer in never smokers exclusively, and results are discrepant. We aim to assess the relationship between residential radon and risk of lung cancer in never smokers in Galicia (Spain), a radon prone area. We designed a multicenter hospital-based case-control study. There are 8 participating hospitals in 2 Spanish regions. To be included all individuals had to fulfill with the WHO definition of never smoker (less than 100 cigarettes in lifetime or less than 1 cig/day during 6 months). Cases and controls have to be older than 30 and a sex and frequency matching with cases was used for controls. Controls were individuals attending hospital for trivial surgery or major ambulatory surgery. All individuals were interviewed by trained personnel with a standardized questionnaire with special emphasis on their lifestyle. A radon detector was given to participants along with placement instructions. The detector was placed for 3 months at the main bedroom of the dwelling. The results are analyzed through logistic regression. Results are expressed as Odds Ratios (OR) adjusted by age, sex and passive smoking. In this analysis we present the results for 121 cases and 117 controls. The participation rates and radon device returning are higher than 90% and very similar among cases and controls. Median radon concentration for cases was 172Bq/m3 versus 152 for controls. Age and sex distribution was very similar between cases and controls. Taking as a reference a residential radon concentration below 100 Bq/m3, the odds ratios (OR) for developing lung cancer for individuals exposed to 101-147 Bq/m3; 148-200Bq/m3 and >200 Bq/m3 were, respectively: 0,7 (95% CI 0,3-1,5); 1,3 (95% CI 0,5-3,1) and 1,2 (95% CI 0,6-2,5). These results do not confirm an association between residential radon and lung cancer in never smokers.

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CRITERION VALIDITY OF THE NTPROBNP IN PATIENTS WITH SEVERE DYSPNEA WITH UNCERTAIN DIAGNOSIS OF ACUTE FEART FAILURE.

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Introduction: Heart failure (HF) is currently a public health problem whose prevalence and incidence has increased in recent years in epidemic proportions. Natriuretic peptides, which are secreted primarily in the heart, might have high diagnostic and prognostic value in HF. The objective of this study was to determine the criterion validity of the amino-terminal fragment of brain natriuretic peptide (NTproBNP) in patients with severe dyspnea with uncertain diagnosis of acute HF compared with Framingham clinical criteria (FCC). Materials and Methods: Assessment of diagnostic technologies. Cross-sectional sampling. The study population consisted of 50 adult patients of three health institutions from Bucaramanga-Colombia, whose admission was for respiratory distress with suspected diagnosis of HF, who underwent the NTproBNP serological test and the FCC were applied to establish the diagnosis of HF. It was calculated the conditional probabilities of NTproBNP: sensitivity, specificity, positive predictive value and negative predictive value. The discriminatory power of NTproBNP was determined by the area under the receiver operating characteristic (ROC) or ROC curve. Results: Sensitivity (92.68%, 95% CI: 80.08% - 98.46%), specificity (88.89%, 95% CI: 51.75% - 99.72%), positive predictive value (97.44%, 95% CI: 86.52% - 99.94%), negative predictive value (72.73%, 95% CI: 39.03% - 93.98%), prevalence of HF (82.00% 95% CI: 68.56% - 91.42%), area under the ROC curve (0.91, 95% CI: 0.79 - 1.00). Conclusions: HF remains an entity with increased prevalence. The findings of this study show good sensitivity and specificity of the NTproBNP for the diagnostic of HF. Health professionals should be know the validity and utility of diagnostic tests.

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BIRTH WEIGHT AND ADULT CARDIOVASCULAR RISK FACTORS USING MULTIPLE BIRTH STATUS IN THE 1958 BIRTH COHORT AS AN INSTRUMENTAL VARIABLE.

*Man Ki Kwok, Siu Lun Au Yeung, Gabriel M Leung, C Mary Schooling (School of Public Health, University of Hong Kong, Hong Kong SAR China)

The effect of birth weight on cardiovascular risk factors is still controversial because it is based on potentially confounded observational evidence, and appears to be contextually specific. Multiple births are largely a random genetic event negatively associated with birth weight but not directly associated with diabetes or cardiovascular disease. The authors evaluated the credibility of multiple birth status as an instrumental variable (IV) for birth weight and obtained IV estimates of the association of birth weight-for-gestational age z-score, relative to the UK-WHO growth charts, with self-reported height and body mass index (BMI) using 2-stage least squares regression and with hypertension and diabetes using probit IV regression at 42 years in the 1958 British birth cohort (n = 9,451). Multiple births (203 twins and 6 triplets) were associated with older maternal age, but not with paternal occupation or maternal smoking. Multiple births had lower birth weight-for-gestational age z-score adjusted for maternal age, with F statistic 145.3 suggesting weak instrument bias is unlikely. Using IV estimates birth weight-for-gestational age z-score was not associated with BMI (0.42 kg/m2, 95% confidence interval (CI) -0.17, 1.01), height (0.01 meter, 95% CI -0.003, 0.02), hypertension (odds ratio (OR) 0.84, 95% CI 0.61, 1.16) or diabetes (OR 1.89, 95% CI 0.93, 3.84). The results were similar when triplets were excluded. Multiple birth status is a credible instrument for birth weight, based on using multiple birth status as an IV, birth weight appeared unrelated to adult cardiovascular risk factors in a long-term developed Western population.

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BIRTH WEIGHT, INFANT GROWTH AND ADOLESCENT BLOOD PRESSURE USING TWIN STATUS AS AN INSTRUMENTAL VARIABLE IN A CHINESE BIRTH COHORT: "CHILDREN OF 1997".

*Man Ki Kwok, Siu Lun Au Yeung, Gabriel M Leung, C Mary Schooling (School of Public Health, University of Hong Kong, Hong Kong SAR China)

The effect of birth weight and infant growth on blood pressure remains controversial because observed associations are open to residual or unmeasured confounding. Instrumental variable (IV) analysis may provide a less confounded estimate. The authors used twin status as an IV in 2-stage least squares regression to obtain IV estimates of the association of birth weight-for-gestational age z-score (relative to standards for contemporary Hong Kong Chinese infants) and change in weight z-score at ages 0-12 months (relative to the 2005 World Health Organization growth standards) with sex-, age- and height-adjusted systolic blood pressure (SBP) and diastolic blood pressure (DBP) at 11 years (n = 6,041) and 13 years (n = 4,708) in Hong Kong's "Children of 1997" birth cohort. Twin birth (n = 89) was more common for older mothers and migrant mothers from the rest of China, but was not associated with socioeconomic position or mother's smoking. Twins had lower birth weight-for-gestational age z-score (F statistic = 38.1) and greater change in weight z-score at 0-12 months (F = 54.1) adjusted for mothers' age and birthplace. Birth weight-for-gestational age z-score was not associated with SBP (0.41 mmHg, 95% confidence interval (CI) -2.13, 2.94) or DBP (0.53 mmHg, 95% CI -1.01, 2.08) at 11 years. Change in weight z-score at 0-12 months was not associated with SBP (-0.13 mmHg, 95% CI -1.70, 1.43) or DBP (-0.22 mmHg, 95% CI -1.18, 0.74) at 11 years. Estimates were similar for blood pressure at 13 years although the F statistic was lower. This IV analysis suggests that birth weight and infant growth make a negligible contribution to adolescent blood pressure.

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WARFARIN ANTICOAGULATION THERAPY AND MORTALITY FOLLOWING GASTROINTESTINAL HEMORRHAGE IN PATIENTS WITH ATRIAL FIBRILLATION IN CLINICAL CARE: THE ATRIA AND ATRIA-CVRN COHORTS.

*Jeffrey Ashburner, Alan Go, Kristi Reynolds, Yuchiao Chang, Margaret Fang, Kate Applebaum, Lisa Fredman, Daniel Singer (Boston University School of Public Health; Massachusetts General Hospital, Boston MA 02114)

Warfarin therapy may be underutilized in patients with atrial fibrillation (AF) for fear of causing hemorrhage. We examined short and long-term mortality of gastrointestinal (GI) hemorrhage, the most common site of bleeding, in AF patients on and off warfarin in clinical care. The sample included patients from the AnTicoagulation and Risk Factors In AF (ATRIA) cohort from Kaiser Permanente (KP) Northern CA, followed from July 1996-September 2003 and the ATRIA-CVRN (Cardiovascular Research Network) cohort from KP Northern and Southern CA, followed from January 2006-June 2009. Validated GI hemorrhages were classified as exposed or unexposed to warfarin. Generalized linear modeling was used to estimate the risk ratio (RR) for the association between warfarin status at the time of GI hemorrhage and 30-day mortality. Cox proportional hazards regression was used to estimate the mortality rate ratio (mRR) over the follow-up period (mean = 1.51 years). All models were adjusted for cohort, age, aspirin use, and history of GI hemorrhage, dementia, and cancer. The sample included 1396 GI hemorrhages, with 747 (54%) exposed to warfarin and 649 (46%) unexposed to warfarin. By 30-days, 6.2% of patients on warfarin had died, compared to 11.9% of those not on warfarin. After 30 days, an additional 36.4% of the sample died. Patients on warfarin had a lower risk of 30-day mortality following any GI hemorrhage than those not on warfarin (RR = 0.57, 95% CI = 0.38-0.84). Similar results were observed in 841 patients with major GI hemorrhage (≥2 blood units transfused) (RR = 0.65, 95% CI = 0.41-1.01). However, warfarin use was not significantly associated with long-term mortality after the 30-days following any GI hemorrhage (mRR = 0.99, 95% CI = 0.81-1.23) or major GI hemorrhage (mRR = 0.88, 95% CI = 0.68-1.14). In summary, warfarin use at the time of GI hemorrhage was associated with a reduced risk of short term mortality, but not in the long term.

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EPIGENETICS AND THE METABOLIC SYNDROME: DNA METHYLATION OF CARDIOVASCULAR DISEASE-RELATED GENES.

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Background: Epigenetic changes associated with regulation of gene expression may be influenced by lifestyle behaviors. This study examined associations between the methylation of targeted cardiovascular disease (CVD)-related genes and metabolic syndrome in older adults. Method: This is a cross sectional study of 492 randomly selected white participants of the Cardiovascular Heart Study (CHS) examined at their baseline in 1989/90. We quantified methylation of 8 CVD-related genes from stored blood samples using a quantitative methylation-specific PCR (QMSP) assay: tumor necrosis factor (TNF); superoxide dismutase 3 (SOD3); synuclein, gamma (SNCG); serpin peptidase inhibitor, clade A, member 5 (SERPINA5); interleukin 10 (IL10); adeno triphosphate binding cassette transporter (ABCA1); uridine triphosphate glucuronyltransferase 1 family, polypeptide A1 (UGT1A1); and nucleotide-binding oligomerization domain 2 (NOD2). Metabolic syndrome was defined as presence of at least three of five factors: waist circumference >102cm(men), >88cm(women); triglyceride level >150mg/d; HDL cholesterol level <40mg/ld. (men), <50 mg/ld. (women); blood pressure >130/85 mm Hg; or fasting glucose >100 mg/ld. Multivariate logistic regression evaluated the associations adjusting for age, gender, education, smoking, alcohol, physical activity, Interleukin-6, fibrinogen and factor VII. Results: Methylation of TNF gene was inversely associated with prevalent metabolic syndrome (Odds ratio(OR):0.9; 95% confidence interval (CI):0.97-0.99; p-value = 0.03) and positively associated with four genes: SOD3 (OR:1.08; 95% CI:1.01-1.14, p = 0.xx); SNCG (OR:1.01, 95% CI:1.001-1.03, p = 0.04); IL10 (OR:1.02, 95% CI:1.001-1.01, p = 0.04); and ABCA1 (OR:1.02, 96% CI:1.01-1.03; p < 0.001). Conclusion: Presence of the metabolic syndrome in older adults was associated with methylation of CVD-protective genes and decreased methylation of TNF, a proinflammatory gene which promotes CVD.

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AMBIENT TEMPERATURE DURING GESTATION AND COLD-RELATED ISCHEMIC HEART DISEASE AND STROKE MORTALITY IN A SWEDISH COHORT, 1915 TO 2002.

*Tim Bruckner, Gerard van den Berg, Kirk Smith, Ralph Catalano (University of California, Irvine, Irvine CA 92697)

For all climatic regions, mortality due to cold exceeds mortality due to heat. A separate line of research indicates that lifespan after age 50 depends on month of birth. This and other literature implies the hypothesis that ambient temperature during gestation may influence cold-related mortality later in life. We use data on over 13,500 Swedes from the Uppsala Birth Cohort Study to test whether cold-related mortality in adulthood varies positively with exposure to unusually benign ambient temperature during gestation. We linked instrument-based, daily temperatures in Uppsala, Sweden (from 1915 to 2002) to subjects beginning at their estimated date of conception and ending at death or the end of follow-up. We specified a counting process Cox proportional hazards model to analyze the two leading causes of cold-related death in adulthood: ischemic heart disease (IHD) and stroke. The counting process model flexibly allows for time-varying exposure to temperatures over the life course. 1,313 IHD deaths and 406 stroke deaths occurred over 540,450 person-years. Cold-related IHD mortality rises among persons exposed to relatively warm gestations. For a one standard deviation increase in warm temperatures during gestation, we observe an increased hazard ratio of 1.16 for cold-related IHD death (95% confidence interval: 1.03—1.29). We, however, observe no relation for cold-related stroke mortality. Additional analyses indicate no effect modification of either result by gender and no mediation of the IHD findings via birthweight or gestational age. To our knowledge, the IHD findings provide the first evidence that ambient temperature during gestation, independent of birth month, modifies the relation between cold and adult mortality.

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CALCIUM PLUS VITAMIN D SUPPLEMENTATION AND THE RISK OF HEART FAILURE: THE CALCIUM AND VITAMIN D TRIAL OF THE WOMEN'S HEALTH INITIATIVE STUDY. *Macarius M Donneyong, Kira C Taylor, Richard N Baumgartner, John Myers, Wenjun Li, Yiqing Song, Lisa W Martin, Eiran Z Gorodeski, James M Shikany, Liviu Klein, Charles Eaton, Carlton A Hornung, JoAnn E Manson (University of Louisville, Louisville KY 40202)

Background: This study evaluates the impact of a randomized intervention with vitamin D plus calcium (CaD) on the prevention of heart failure (HF) in post-menopausal women (PW). It also tests whether baseline cardiovascular risk status modifies the effect of the intervention on HF risk. Methods: The Women's Health Initiative (WHI) CaD trial tested 1,000 mg/day calcium plus 400 IU/day vitamin D3 in PW who were 50 to 81 years of age at randomization. Analyses were restricted to 35,113 women (17,595 intervention, 17,518 placebo), who were free of HF at time of randomization. HF cases over a mean follow-up period of 7.13 (SD, 1.33) years were assessed from hospital discharge records and adjudicated. Intention-to-treat approach was used to estimate hazard ratios (HR) and 95% confidence intervals (CI) from Cox regression models. A formal test of interaction between CaD and baseline cardiovascular risk status (high and low) was performed. The high risk population (n = 17,016) included those who reported pre-existing hypertension, cardiovascular diseases, coronary heart diseases/events, or diabetes at baseline, while the low risk group (n = 8,097) did not report any of these conditions. Results: CaD was associated with a non-significant reduced risk of HF (HR = 0.92; 95% CI, 0.79 –1.06), compared to placebo, in the overall cohort. There was a significant (P = 0.01) interaction between CaD and baseline cardiovascular risk status. CaD was associated with a reduced risk of HF in the low risk (HR = 0.65; 95% CI, 0.46 – 0.92; P = 0.01) but not in the high risk population (HR = 1.02; 95% CI, 0.85 – 1.21). These effect estimates were not modified by baseline total intake of calcium or vitamin D (diet plus supplements). Conclusion: Baseline cardiovascular risk status modified the effect of CaD supplementation on risk of HF in PW. CaD was associated with a reduced risk of HF in the population at low risk while its effect in the high risk and overall study population was inconclusive.

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HEIGHT, ITS COMPONENTS, AND HEMATOLOGICAL COAGULABILITY AMONG OLDER CHINESE: THE GUANGZHOU BIOBANK COHORT STUDY. *Yi Zhong, CQ Jiang, KK Cheng, W Zhang, TH Lam, GM Leung, CM Schooling (School of Public Health The University of Hong Kong, Hong Kong SAR China)

With new discoveries in genetics and failed randomized controlled trials (RCT) increasingly challenging the causal role of some cardiovascular risk factors, such as HDL-cholesterol and fasting glucose, in cardiovascular disease attention has returned to all the elements of Virchow's triad including hypercoagulability, corroborated by a recent RCT showing reducing hematocrit protected against cardiovascular events. We used multivariable linear regression to assess whether childhood influences, proxied by height and its components, existed for hematocrit (HCT), hemoglobin (HGB) and platelets (PLT) in 28595 older Chinese adults (mean age = 61.8 years) from the Guangzhou Biobank Cohort Study. Adjusted for age and sex, leg length was negatively associated with HCT (-0.011% per cm, 95% confidence interval (CI) -0.02 to -0.001), and PLT (-0.95 $*10^9$/L per cm, 95% CI -1.14 to -0.77). Sitting height and height were positively associated with HCT (0.06% per cm, 95% CI 0.05 to 0.07 for sitting height; 0.02% per cm, 95% CI 0.009 to 0.023 for height) and HGB (0.21g/L per cm, 95% CI 0.16 to 0.25; 0.06 g/L per cm, 95% CI 0.03 to 0.08) and negatively associated with PLT (-1.1 $*10^9$/L per cm, 95% CI -1.3 to -0.84; -0.84 $*10^9$/L per cm, 95% CI -0.97 to -0.72). Sitting height-to-leg ratio was positively associated with HCT (2.4% per cm, 95% CI 1.8 to 2.9), HGB (2.4 g/L per cm, 95% CI 1.8 to 2.9) and PLT (15.8 $*10^9$/L per cm, 95% CI 5.9 to 25.6). Further adjustment for potential confounders, such as education, smoking and alcohol use little changed the estimates. For the first time we provide anthropometric evidence for the role of pre-pubertal and pubertal exposures in coagulability. Whether factors that promote pre-pubertal and reduce pubertal growth may help to prevent cardiovascular events, via effects on coagulability, overall or in specific sub-groups, such as those with pre-existing disease, remains to be determined.

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PROGNOSTIC VALUE OF N-TERMINAL PRO-BRAIN NATRIURETIC PEPTID (NT_PROBNP) TRAJECTORIES IN PATIENTS WITH STABLE CORONARY HEART DISEASE. *Dhayana Dallmeier, Michael Pencina, Hermann Brenner, Ute Mons, Wolfgang Koenig, Dietrich Rothenbacher (University of Ulm, Ulm Germany)

There is sparse information about the prognostic value of NT-proBNP trajectories in patients with stable coronary heart disease (CHD). We examined a NT-proBNP three-year course and its prognostic value on subsequent cardiovascular events (CVE) in patients with CHD. NT-proBNP was measured at the end of rehab (baseline), at one and three years follow-up in a cohort of patients aged 30-70 years participating in an in-hospital cardiac rehabilitation (median follow-up for a secondary CVE 7 years). NT-proBNP values were log-transformed. We estimated individual regression lines for NT-proBNP trajectories. We evaluated their prognostic value in relation to subsequent secondary CVEs (myocardial infarction, stroke, cardiovascular death) by adding the obtained intercepts and slopes in a Cox proportional hazards model containing baseline values of established prognostic factors (PF): age, sex, body mass index, smoking, left ventricular function, number of affected vessels, history of diabetes / heart failure, statin / aspirin use. There were 80 secondary CVEs among 641 participants (84% men, mean age 59.6 years). Median NT-proBNP levels were high at baseline (568.8 pg/mL) showing a falling trend over time (191.5 and 172 pg/mL at one and three years follow-up respectively). In the multivariable analysis an increase of the slope by 0.1 per unit log-NT-proBNP was associated with a Hazard Ratio of 1.26 (95% confidence interval 1.15, 1.37) for the onset of a secondary CVE. Adding NT-proBNP trajectories to the model with established PFs provided a net reclassification improvement of 35.5% (18% and 17.5% among those with and without a CVE respectively) for the risk strata of 5, 10 and >20% predicted probability. NT-proBNP three-year course remained as an important PF for secondary CVEs independent of NT-proBNP baseline values and established cardiovascular PFs, and therefore could help to guide risk stratification and clinical management among patients with stable CHD.

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REMITTED DEPRESSIVE SYMPTOMS AND SUBSEQUENT STROKE RISK: CONTRASTING MARGINAL STRUCTURAL MODELS AND CONVENTIONAL MODELS. *Paola Gilsanz, Stefan Walter, Kristen K Patton, J Robin Moon, Benjamin Capistrant, Jessica Daniel, Laura Kubzansky, Ichiro Kawachi, M Maria Glymour (Harvard School of Public Health, Boston MA 02115)

Background: Elevated depressive symptoms (DS) predict stroke, but it is unclear if stroke risk remains elevated after remission of DS. Conventional survival models may be inadequate to control for time varying factors that act as both confounders and mediators. Methods: Participants in the Health and Retirement Study with no history of stroke (self-report of doctor's diagnosis) at baseline (n = 16,284) were interviewed biennially from 1998-2010. At each interview wave, elevated DS were defined as scores of 3+ on the 8-item Centers for the Epidemiologic Study of Depression scale. Remitted DS were defined as elevated DS at one wave followed by non-elevated DS at the next wave. Using discrete time survival models, we compared individuals with remitted DS to those with low/no DS levels at two successive waves (stable non-elevated DS) for prediction of incident stroke (1,397 events) during the subsequent 2 year interval. Invariant covariates include baseline values of demographics and DS. Time varying covariates include age, marital status, income, wealth, health behaviors, and health conditions. Conventional models statistically accounted for time varying and invariant covariates through direct regression adjustment. Marginal structural models (MSM) accounted for time varying confounders (including DS at prior wave), censoring, and survival through inverse probability weighting (IPW). All models incorporated survey sampling weights. Results: Conventional models indicated no significant differences in the adjusted hazard ratio (aHR) of incident stroke for individuals with remitted DS compared to those with stable low/no DS (aHR = 1.00; 95% CI: 0.76, 1.32), whereas in MSM models, remitted DS predicted significantly elevated stroke risk (aHR = 1.82; 95% CI: 1.36, 2.42) compared to those with stable low/no DS. Conclusions: Remitted DS predict elevated 2-year stroke risk in MSM models with IPWs to account for time-varying confounding and sample attrition.

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VEGETARIAN DIETARY PATTERNS AND CARDIOVASCULAR RISK FACTORS AMONG BLACK SUBJECTS IN THE AHS-2 COHORT. *Gary Fraser, Jing Fan, Ramtin Anousheh, Sozina Katuli, Patti Herring (Loma Linda University, Loma Linda CA 92350)

Although plant-based diets are associated with lower risk values of many cardiovascular risk factors in White subjects, there is much less information about such associations in Blacks. About 25% of subjects in the Adventist Health Study-2 cohort are Black, and they come from all states of the U.S. We have used two sub-studies, where subjects attended clinics, to investigate associations between vegetarian dietary patterns and several cardiovascular risk factors in 595 Black subjects. 27 items from an extensive food frequency questionnaire enables categorization of subjects to non-vegetarian(N = 368), pesco-vegetarian(N = 86), or the combined category of lacto-ovo- and vegan vegetarians (labeled L-O/vegans, N = 141). For diagnoses of hypertension, diabetes, or hyperlipidemia, account was taken of measured blood pressures, fasting glucose, or fasting lipids, but in addition whether medications were taken for these disorders. When non-vegetarians are the reference category, and adjusting for age, gender, and education, the following odds ratios (95% confidence intervals)were found for L-O/vegans: Hypertension 0.61(0.39,0.94); Diabetes 0.46(0.24,0.90);High cholesterol 0.45(0.30,0.70); High LDL 0.52(0.34,0.81); Obesity 0.44 (0.28,0.67); High waist circumference 0.55(0.37, 0.84). For pesco-vegetarians, the only significant differences from non-vegetarians were for obesity with an OR of 0.43 (0.25,0.73) and high waist circumference with OR of 0.46 (0.28,0.76). In conclusion, among Black subjects also, there appears to be sizeable advantages to a vegetarian dietary pattern, although we cannot discriminate between vegan and lacto-ovo vegetarian with this data.

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ADIPOKINES, INFLAMMATORY, AND COAGULATION FACTORS IN METABOLIC SYNDROME AMONG RURAL AND URBAN INDIAN MEN. *Ananya Roy, Adrienne Ettinger, Himangi Lubree, Dattatray Bhat, Charu Joglekar, John Yudkin, Chittaranjan Yajnik (Yale School of Public Health, New Haven CT 06510)

Background: The last decade has seen a rapid rise of cardio-metabolic disease in transition countries, such as India, yet it is unclear what predisposes risk in this population. Methods: The Coronary Risk of Insulin Sensitivity in Indian Subjects(CRISIS) Study investigated relationships between metabolic/cardiovascular risk and adipocytokines, inflammatory and procoagulant markers. Male subjects, age 30-50 years, without preexisting disease, were selected by multistage random sampling from 3 areas (N = 150 each from: rural, slum, urban) in and around Pune, India. Metabolic syndrome (MetS) was determined using the 2009 International Diabetes Federation definition. Multivariate generalized estimating equations, adjusting for age, smoking, diet, physical activity, SES, adiposity and clustering by location, were used to examine associations between leptin, and inflammatory and coagulation factors and MetS. Results: 79 (17.5%) men met the criteria for MetS. Residence in urban and slum areas, respectively, were associated with an OR: 4.5 (95% CI 1.4, 13.8) and OR: 6.6 (95% CI 2.3, 18.9) of MetS in comparison to living in a rural area. Independent of location, a one-SD change in the following markers were associated with higher odds of MetS: leptin (OR: 2.37, 95% CI 1.73, 3.25); IL6 (OR: 1.15, 95% CI 1.03, 1.29), H. pylori IgG (OR: 1.08, 95% CI 1.05, 1.11), WBC (OR: 1.52; 95% CI: 1.28,1.80) PAI1 (OR: 3.14, 95% CI 2.78, 3.54), platelets (OR: 1.33, 95% CI 1.10, 1.61) and e-Selectin (OR: 1.66, 95% CI 1.14, 2.42). No significant associations were seen with CRP, TNFα, fibrinogen and vWF. These markers explained approximately 20-40% of the variation in the components of MetS after accounting for most known risk factors. Conclusions: Leptin, inflammatory and coagulation markers are associated with MetS, yet a large amount of unexplained variation remains, suggesting that environmental factors, not measured in the study, may also contribute to risk of MetS.

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HEALTH BEHAVIOR, ACCESS TO CARE, AND ATTITUDES REGARDING EMERGENCY SITUATIONS AND THE USE OF 911 AMONG REACH MUSC TELESTROKE CONSULTS. *Angela M Malek, Robert J Adams, Ellen Debenham, Hyacinth I Hyacinth, Daniel T Lackland (Medical University of South Carolina, Charleston SC 29425)

Background: Race/ethnicity has been associated with differences in response to a stroke event. Remote Evaluation of Acute isCHemic stroke (REACH) MUSC is a telestroke network which has provided >3,000 consults in South Carolina with the aim of improving access to quality acute stroke care. However, patients often arrive at local emergency departments (EDs) too late for tissue Plasminogen Activator (tPA). We used the experience of a sample of consults to try to learn more about response to stroke symptoms, and especially the use of 911, in an effort to design interventions to speed patient arrival to telemedicine equipped EDs after stroke. Methods: Letters were sent to 627 of the 2,325 REACH consults describing the telephone survey. Of these, 197 (31%) completed the survey, while among non-respondents, 11% had wrong addresses, 13% were deceased, 1% were in nursing homes, 11% refused to participate, 2% hung up, 13% could not be reached after 10 attempts, 32% had disconnected numbers, 11% had wrong numbers, and 6% did not have a number. The phone surveys were conducted by trained interviewers from March 2012–January 2013 to evaluate symptoms, attitudes regarding emergencies, and related characteristics of the stroke/event that led to the ED visit. Results: The majority of respondents were Caucasian (71%) and 26% were African-American. Fifty-four percent of participants were male. African-Americans were significantly younger than Caucasians (62.1 + 17.1 vs. 67.8 + 13.3 years, $p < 0.05$) with the majority of African-Americans aged ≤65 years. Eighty percent of African-Americans and 75% of Caucasians thought the event was an emergency, of which 76% and 59% (respectively) called 911. The large majority of African-Americans (90%) and Caucasians (85%) called 911 in <30 minutes. Conclusions: Younger African-Americans were more likely to have stroke or stroke-like symptoms. In addition, more African-Americans used 911 emergency services compared to Caucasians.

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PREDICTORS OF RISK AND PROTECTION FOR HYPERTENSION IN YUP'IK PEOPLE FROM SOUTHWEST ALASKA. *Eric Roberts, Scarlett Hopkins, Bert Boyer, Jim Allen, Bernadette Boden-Albala (Mount Sinai School of Medicine, New York NY 10029)

Hypertension (HT) is a powerful contributor to vascular disease, and is increasingly common in non-western, rural contexts, such as the Yup'ik people of Southwestern Alaska. While much is known regarding HT risk factors in western contexts, little is known about their relevance to non-western populations. This work explores an American Heart Association risk factor model for HT in predicting risk and protection from HT among Yup'ik people. Using data from 1015 Yup'ik individuals residing in remote Southwestern Alaska, we explored age, sex, education, waist, physical activity, tobacco, social support, and cultural identification and odds of definitive hypertension (def-HT; blood pressure ≥140/90 mmHG). Age (one year increase; odds ratio (OR) = 1.05, 95% Confidence Interval (CI)1.03, 1.07), waist (one cm increase; OR = 1.03, 95% CI 1.01, 1.05), ever smoking (OR = 2.06, 95% CI 1.24, 3.41), and use of HT medications (OR = 1.88, 95% CI 1.07, 3.29) were associated with def-HT. In multinomial logistic regressions comparing pre-hypertension (pre-HYPT; systolic 120 to 129 mmHg), and hypertension (HYPT; systolic ≥130 mmHg) to optimal blood pressure (opt-BP; systolic < 120 mmHg) we also found men have 86% (95% CI 57, 121) greater odds of pre-HYPT, people with fasting blood glucose ≥110 mg/dl have 52% (95% CI 3, 122)) increased odds of pre-HYPT, and married persons have 19% (95% CI 1, 34) lower odds of having pre-HYPT compared to having opt-BP. Interactions between cultural identification with age, and education were assessed. We find bicultural indentifcation protects against age related increases in blood pressure and blunts the effect of low formal education. While continuities with the AHA risk factor model were noted in our Yup'ik study, important points of divergence were also noted. Future research on cultural identification and social support has promising implications for guiding responsive interventions.

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COMBINED LOW-RISK DIETARY AND LIFESTYLE PRACTICE AND RISK OF MYOCARDIAL INFARCTION IN MEN. *Agneta Åkesson, Susanna Larsson, Alicja Wolk (Karolinska Institutet, Stockholm Sweden)

Background: Limited data are available on the benefit of combining healthy dietary and lifestyle practice in the prevention of coronary heart disease (CHD) in men. We identified a low-risk behavior in men and examined its association with incidence of primary myocardial infarction. Methods and Results: The population-based prospective Cohort of Swedish Men, is based on 45 to 79 year-old men who completed a detailed questionnaire on diet and lifestyle at baseline (1998). We included 27,696 men with no history of cancer, cardiovascular disease, diabetes, hypertension or high cholesterol levels. The low-risk practice included a healthy diet (top quintile of Recommended Food Score), moderate alcohol consumption (≥10 g/day; median 18 g/d), no history of smoking, being physically active (walking/bicycling ≥40 minutes/day and exercising ≥1 hour/week) and having no abdominal adiposity (waist circumference <95 cm). During average 11 years of follow-up, we ascertained, by linkage to national patient-registers, 1835 incident cases of myocardial infarction. The low-risk dietary choice together with a moderate consumption of alcoholic beverages was associated with a relative risk (RR) of 0.59 (95% confidence interval, CI 0.47-0.75) of MI compared to men with no low-risk factors. Men having all 5 low-risk factors compared to those with no low-risk factors had a RR of 0.15 (95% CI, 0.04-0.59). This combination of healthy behaviors, present in 0.5% of the men, may prevent 78% (95% CI, 14-95%) of the coronary events in the study population. Conclusion: A combined low-risk diet and lifestyle may prevent about 4 out of 5 cases of MI in the study population.

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THE ASSOCIATION BETWEEN WATER INTAKE AND CORONARY HEART DISEASE MORTALITY. RESULTS FROM THE ADVENTIST HEALTH STUDY-2. *Abdullah Marghalani, Larry Beeson, Raymond Knutsen, Synnove Knutsen (Loma Linda University, School of Public Health, Loma Linda CA 92350)

Objective: We have previously reported an inverse relationship between frequent water intake and fatal CHD in the Adventist Health Study-1. This study attempts to verify earlier findings using a similar, but larger cohort, the Adventist Health Study-2 (AHS-2). Materials and Methods: Study subjects were part of the AHS-2, a prospective cohort study of 96,000 subjects from USA and Canada. Subjects with a history of heart attack at baseline were excluded giving us an analytic population of 88,843 males and females aged 30+ at baseline. Subjects completed a large baseline questionnaire which included medical history, a food-frequency section including water and other fluids intake, physical activity, use of certain medications, a female section and a demographic section. Mortality information was obtained from record linkage with the National Death Index. Risk of CHD death (ICD_10 codes: I20 – I25) was assessed using Cox-proportional hazard regression analysis with "attained age" as the time variable. Results: A total of 729 subjects died from CHD during follow-up (2002-09), 47.47% males and 52.53% females. A protective effect of water intake on CHD mortality was observed. Compared to subjects who reported drinking water one time or less per day, those drinking water 2-3 times, 4-5 times and 6+ times per day had 22% (RR = 0.78, 95% CI: 0.62, 0.99), 22% (RR = 0.78, 95% CI: 0.64, 0.97), and 21% (RR = 0.79, 95% CI: 0.64, 0.97) lower risk, respectively, of dying from CHD after adjusting for gender, race, exercise, smoking, education, body mass index, hypertension and hypercholesterolemia. Other known risk factors for CHD mortality were similar in our study to what has been reported from other studies. Conclusion: Our findings confirm earlier findings from the AHS-1, that frequent water intake is associated with lower CHD mortality. Further studies, from other cohorts, would be useful to confirm our findings.

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FOREST FRAGMENTATION AND THE RISK OF BABESIOSIS: INVESTIGATING THE LANDSCAPE EPIDEMIOLOGY OF AN EMERGING TICK-BORNE DISEASE. *Michael Walsh (New York University, New York, NY 10003)

Babesiosis is an emerging arthropod-borne infection that has been increasing in incidence for the last decade in the northeastern United States. Babesiosis may share features of its landscape epidemiology with other, more common, arthropod-borne infections transmitted by the same tick vectors in similar geographic spaces. This study examined 11 years of surveillance data in New York State to measure the relationship between forest fragmentation and the incidence of human babesiosis. Adjusted Poisson models showed that increasing edges of contact between forested land and developed land, as measured by their shared perimeters, was associated with a higher incidence of babesiosis cases (incident rate ratio (IRR) = 1.03, 95% C.I. 1.01 – 1.04; $p < 0.001$), even after controlling for the total developed land area and forest density, and temperature and precipitation. Each 10 mile increase in perimeter contact between forested land and developed land per county was associated with a 3% increase in babesiosis risk. While direct causal conclusions cannot be drawn from these data, these findings do identify a potentially important signal in the epidemiology of babesiosis and suggest that the underlying physical landscape may play a role in shaping points of contact between humans and tick vectors and the subsequent transmission of Babesia microti.

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POSTLICENSURE SAFETY SURVEILLANCE FOR 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE. *Hung Fu Tseng, Lina Sy, Amy Liu, Lei Qian, S Michael Marcy, Eric Weintraub, Katherine Yih, Roger Baxter, Jason Glanz, James Donahue, Allison Naleway, James Nordin, Steven Jacobsen (Kaiser Permanente Southern California, Pasadena CA 91101)

Background: Although no increased risk was detected for serious adverse events in the prelicensure trials for the 13-valent pneumococcal vaccine, Prevnar 13® (PCV13), PCV13, continued monitoring of rare but serious adverse events is necessary. Methods: A surveillance system using cohort study design was set up to monitor safety of PCV13 immediately after it was included in the childhood immunization program in the United States. The exposed population included children 1 month to 2 years old who received PCV13 from April, 2010 to January, 2012 from the eight managed care organizations participating in the Vaccine Safety Datalink project in the United States. The historical unexposed population was children of the same age who received the 7-valent pneumococcal conjugate vaccine Prevnar 7® (PCV7) in 2007 (or 2005 depending on outcome of interest) to 2009. The risk of pre-specified adverse events in the risk window following PCV13 were repeatedly compared to that in the historical comparison group. Results: The number of doses included in the study was 599,229. No increased risk was found for febrile seizures, urticaria or angioneurotic edema, asthma, thrombocytopenia, or anaphylaxis. An increased risk for encephalopathy was not confirmed following medical record review. The relative risk for Kawasaki disease in 0-28 days following vaccination was 1.94 (95% Confidence interval: 0.79-4.86), comparing PCV13 to PCV7. Conclusion: We identified no significant increased risk of pre-specified adverse events in the Vaccine Safety Datalink study cohort. The possible association between the 13-valent pneumococcal conjugate vaccine and Kawasaki disease may deserve further investigation.

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EFFECT OF VITAMIN D SUPPLEMENTATION ON ANTIBIOTIC USE AND UPPER RESPIRATORY TRACT INFECTION: A RANDOMISED CONTROLLED TRIAL. *Rachel Neale, Bruce Armstrong, Peter Ebeling, Dallas English, Michael Kimlin, Jolieke van der Pols, Alison Venn, Val Gebski, David Whiteman, Penelope Webb, Bich Tran (Queensland Institute of Medical Research, Brisbane QLD Australia)

Background: Observational data suggest that supplementation with vitamin D could reduce the risk of infection but trial data are inconsistent. We aimed to examine the effect of oral vitamin D supplementation on antibiotic use and upper respiratory tract infection (URTI). Methods: The study was nested within a randomized pilot trial of vitamin D supplementation (Pilot D-Health) carried out in a general community setting between October 2010 and February 2012. We recruited 60-84 year-old residents of one of the four eastern Australian states who did not have any vitamin D-related disorders and who were not taking more than 400 IU of supplementary vitamin D per day. 644 participants were randomized to monthly doses of placebo (N = 214), 30,000 (N = 215) or 60,000 IU (N = 215) of oral cholecalciferol for 12 months. At the end of the intervention period we asked participants to report symptoms of URTI in the previous 12 months. Antibiotics prescribed during the intervention period were ascertained by linkage with pharmacy records through the national health insurance scheme (Medicare Australia). Results: In an intention-to-treat analysis people randomised to 60,000 IU cholecalciferol were at a nonsignificantly lower risk than the placebo group of being prescribed antibiotics at least once (relative risk (RR) = 0.72, 95% CI 0.48-1.07); in those aged 70 years and over the RR of antibiotic use was 0.53 (95% CI 0.32-0.90). There was a non-significant inverse association between vitamin D supplementation at 60,000 IU per month and self-reported URTI (RR = 0.78, 95% CI 0.53-1.15). Conclusions: These data are consistent with the hypothesis that high dose vitamin D supplementation reduces the incidence of infection, particularly in people aged over 70 years.

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IMPACT OF EL NINO SOUTHERN OSCILLATION ON INFECTIOUS DISEASE HOSPITALIZATION RISK IN THE UNITED STATES, AND IMPLICATIONS FOR CLIMATE CHANGE. *Sandy Bae, Ashleigh Tuite, Kevin Brown, David Fisman (Dalla Lana School of Public Health, University of Toronto, Toronto ON Canada)

Introduction: Although the global climate is changing at an unprecedented rate, links between weather and infectious disease have received little attention in high-income countries. The "El Nino Southern Oscillation" (ENSO) results in climatic changes similar to those anticipated with long-term climate change. We studied the impact of ENSO on infectious diseases in the United States. Methods: We evaluated infectious diseases requiring hospitalization using the U.S. National Hospital Discharge Survey (1970-2009) and disease groupings expected to undergo an epidemiological shift with changing climate: (i) pneumonia and influenza; (ii) gastroenteritis; (iii) tick-borne/rickettsial diseases; and (iv) arthropod-borne viral diseases. ENSO activity was evaluated for multiple ENSO indices, with the NOAA Multivariate ENSO Index used in the base case. Distributed lag models, with adjustment for seasonal oscillation and long-term trends, were used to evaluate the impact of ENSO on disease incidence over lags of 12 months or less. Results: Hospital admissions due to gastroenteritis and tick-borne/rickettsial diseases were associated with El Nino events in some regions of U.S. Risk for gastroenteritis increased in the Northeast (relative risk (RR) = 1.15 (95% CI 1.01-1.31)) and decreased in the West (RR = 0.73 (0.62-0.87)). We observed an increased risk for tick-borne/rickettsial diseases in the West (RR = 5.14 (1.09-24.31)). Observations were robust when alternate ENSO indices were evaluated. We found no associations between ENSO and arthropod-borne viral disease or pneumonia and influenza. Conclusions: We identified regional changes in risk of gastroenteritis and tick-borne infectious disease associated with ENSO activity in the United States. Observed effects are consistent with the regional impact of ENSO on temperature and precipitation, and may serve as a useful model for forecasting climate change impacts on infectious diseases.

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HELICOBACTER PYLORI EXPOSURE AND THE RISK OF NEPHROPATHY IN THE U.S. POPULATION, NHANES 1999-2000. *Helen Meier, Allison Aiello (University of Michigan School of Public Health, Ann Arbor MI 48109)

Background: Exposure to H. pylori, a persistent bacterial infection, is associated with various chronic diseases, and may play a role in both onset and progression of conditions resulting from diabetes. In one such complication, nephropathy, it is thought that H. pylori infection may contribute to inflammation and endothelial damage in the glomerulus and vasculature. Methods: We performed a cross-sectional study using the National Health and Nutrition Examination Survey 1999-2000 to investigate the association between H. pylori exposure and nephropathy. Exposure was determined by serostatus, either seronegative or seropositive. Nephropathy was determined in two ways, albumin-to-creatinine ratio (ACR) ≥30mg/g and glomerular filtration rate (GFR) <60mL/min/1.73m2. Covariates included age, race/ethnicity, and education. Multivariate logistic regression accounting for the complex survey design estimated the odds of nephropathy in the U.S. population. Analyses were repeated in racial subpopulations and among diabetics. Analyses were performed in Stata 12 (College Station, TX). Results: In unadjusted models, seropositive individuals had 1.54 times the odds of nephropathy by ACR than seronegatives (95% CI 1.25 to 1.89), additionally, seropostivies had 1.76 times the odds of nephropathy by GFR than seronegatives (95% CI 1.27 to 2.44). These associations were attenuated and no longer statistically significant after controlling for confounders. Associations between serostatus and nephropathy were observed in subpopulation analyses of race and diabetes; the effects were not statistically significant in adjusted models. Conclusion: In this cross-sectional study, no statistically significant association was observed between H. pylori seropositivity and nephropathy in the U.S. population after adjusting for confounders.

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THE IMPACT OF PRISON INMATE MOVEMENT ON METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS TRANSMISSION IN THE NEW YORK STATE CORRECTIONAL SYSTEM. *Carolyn Herzig, Anne-Catrin Uhlemann, Christie Jeon, Caroline Lee, Benjamin Miko, Dhritiman Mukherjee, Montina Befus, Haomiao Jia, Elaine Larson, Franklin Lowy (Columbia University, New York NY 10032)

Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are an increasing problem in correctional settings. Male inmates enter the New York State (NYS) prison system through reception centers and remain transient with about 100,000 transfers between prisons per year. Recent studies have shown that patient sharing between hospitals is correlated with the spread of infectious disease. However, the impact of prison inmate movement on MRSA dissemination remains unexamined. Linear regression and Mantel's permutation tests were used to evaluate whether the proportion of inmates transferred between prison pairs, based on NYS inmate transfer data, was associated with reduced genetic diversity of their MRSA clinical isolates (a surrogate measure of MRSA spread). The analysis included 378 prison pairs and 138 isolates comprising 23 spa types. In an unadjusted model, increased inmate transfer was associated with reduced genetic diversity between MRSA isolates from prison pairs ($\beta = -0.063$, $p = 0.03$). In an adjusted model, inmate transfer no longer predicted reduced genetic diversity. However, MRSA isolates were more similar from prison pairs in which one ($\beta = -1.096$, $p < 0.001$) or both ($\beta = -2.532$, $p < 0.001$) prisons had a reception center compared with prison pairs with no reception center. Whole genome sequencing (WGS) was used to further characterize 10 USA300 isolates (the most common cause of infection) from one prison with high inmate transfer and one prison with low inmate transfer. Based on phylogenetic analysis of WGS, USA300 isolates from the prison with high transfer were more diverse than those from the prison with low transfer. Together, these findings suggest that inmate transfer and reception centers contribute to MRSA transmission in the NYS prison system. These previously unidentified factors imply that intervention strategies that effectively address and prevent MRSA spread in correctional systems will require a system wide approach.

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WITHDRAWN

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EXAMINING THE ROLE OF HAND CONTAMINATION AND ASYMPTOMATIC COLONIZATION IN THE TRANSMISSION OF HEALTHCARE-ASSOCIATED INFECTIONS. *Eric Lofgren, Rebekah Moehring, David Weber, Nina Fefferman (University of North Carolina, NC 20008)

Healthcare-associated infections (HAIs) are an important source of morbidity and mortality, and represent a major burden on the healthcare system in developed nations. Many of these infections are both avoidable and difficult to treat, fostering interest in interventions to prevent infections from occurring in the first place, rather than relying on new or novel treatment regimens. Hospitals are difficult environments in which to conduct observational research. Patients are not independent from one another, most interventions are not implemented singly but as part of a bundle of efforts to halt outbreaks or reduce endemic rates, and research understandably often takes a secondary role to clinical interventions. Mathematical models of infectious diseases can alleviate some of these problems, allowing for empirical, repeatable research to be conducted in a simulated environment. We used a stochastic compartmental model, simulated using Gillespie's Direct Method to simulate the spread of Clostridium difficile infection (CDI) in an intensive care unit (ICU). Using parameters obtained from both the literature and infection control surveillance data from the Duke Infection Control Outreach Network (DICON), we consider the model's implications for the growing infection control problem of CDI. The results of the model suggested that increased hand hygiene measures may not be effective in decreasing the transmission of CDI, as transmission can be sustained in the model based only on transient, short-lived contamination, with few healthcare workers having contaminated hands for any substantial periods of time. Additionally, our results indicated that there is a considerable burden within the ICU of patients who, while they might lack the risk factors to develop active CDI infection may be colonized with the organism, providing a source for transmission that is difficult to ascertain or control.

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SPATIAL EPIDEMIOLOGY OF HIV-HEPATITIS CO-INFECTION IN THE STATE OF MICHIGAN. *Zahid Butt, Sue Grady, Melinda Wilkins, Elizabeth Hamilton, David Todem, Joseph Gardiner, Mahdi Saeed (Michigan State University, East Lansing, MI 48824)

HIV infected individuals are at an increased risk of acquiring hepatitis B and C viral infections because of shared transmission routes. The purpose of this study was to investigate the geography of HIV and hepatitis co-infection in Michigan using data from the enhanced HIV/AIDS Reporting System (eHARS) and the Michigan Disease Surveillance System (MDSS) of the Michigan Department of Community Health. Retrospective cohort data on HIV infected individuals were matched to all hepatitis B and C cases in Michigan during the period of January 1, 2006 through December 31, 2009. Spatial clusters of HIV and hepatitis B or C co-infection were detected using SaTScan's Bernoulli and discrete Poisson models. Bernoulli cluster analysis of HIV and hepatitis co-infection identified a most likely cluster, relative risk (RR) = 1.75 (P = 0.005) in the northern Lower and Upper Peninsulas. Poisson cluster analysis identified a most likely cluster, RR = 2.93 (P = 0.05) controlling for sex, age and HIV/AIDS status in the western and northwestern Lower Peninsula. Four counties (Newaygo, Lake, Benzie, Leelanau) overlapped in both models indicating 'hotspots' for HIV and hepatitis co-infection. This study identified significant clusters of HIV-hepatitis B and C co-infection in counties that would not be considered high risk because of low population density and low HIV prevalence. In this respect, spatial cluster analysis serves as an important tool to delineate infectious disease clusters, which could be missed by other analytic methods that do not consider geography. The findings from this study may be used to target future public health policy and health care interventions for co-infection in these areas.

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PERSISTENT PATHOGENS AND INCIDENCE OF ELEVATED DEPRESSIVE SYMPTOMS AMONG A LONGITUDINAL COHORT OF ELDERLY LATINOS. *Amanda Simanek, Mary Haan, Shu Chen, Caroline Cheng, Allison Aiello (University of Michigan, School of Public Health, Department of Epidemiology, Center for Social Epidemiology and Population Health, Ann Arbor MI 48109)

Objective: While research has linked persistent pathogens to mental health outcomes, few studies have examined these relationships longitudinally. We examined whether seropositivity for and/or increased antibody levels against cytomegalovirus (CMV), herpes simples virus-1 and -2 (HSV-1 and -2), Varicella zoster (VZV), *Helicobacter pylori* (*H. pylori*) and *Toxoplasma gondii* (*T. gondii*) were associated with greater incidence of elevated depressive symptoms among elderly Latinos in the Sacramento Area Latino Study of Aging (SALSA). Furthermore, we assessed whether these associations were mediated through elevated levels of the pro-inflammatory markers, interleukin-6 (IL-6) and/or C-reactive protein (CRP). Methods: Of the total 1789 SALSA participants, 428 were tested for pathogen seropositivity and IgG antibody titer levels at baseline and were assessed for presence of elevated depressive symptoms (score $\geq$ 16) using the Center for Epidemiologic Studies Depression Scale at baseline and in 6 waves of follow-up over nine years. Negative binomial regression was used to examine the association between pathogen seropositivity/IgG antibody levels, inflammatory marker levels and incidence of elevated depressive symptoms over time. Results: CMV seropositivity at baseline was associated with 1.61 (95% confidence interval 1.05-2.48) times greater incidence of reporting elevated depressive symptoms over 6 waves of follow-up in models adjusted for age, gender, education level, nativity status, acculturation and antidepressant medication use. This association was not mediated by elevated levels of IL-6 or CRP. Conclusions: CMV was the only persistent pathogen for which seropositivity was associated with increased incidence of reporting elevated depressive symptoms over time. Future research should work to elucidate the biologic mechanisms by which CMV infection impacts risk for depression among elderly individuals.

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ASSOCIATION BETWEEN UNPROTECTED UV EXPOSURE AND OCULAR HERPES SIMPLEX VIRUS RECURRENCE.

*Christina Ludema, Stephen Cole (University of North Carolina, Chapel Hill, Chapel Hill NC 27606)

Laboratory and observational studies have suggested that ultraviolet (UV) light exposure may increase the risk of herpes simplex virus (HSV) recurrence. The Herpetic Eye Disease study (HEDS) randomly assigned 703 participants with ocular HSV to twice-daily oral acyclovir or placebo to prevent ocular HSV recurrence. A total of 308 HEDS participants (48% female, 85% white, median age 49 years) were included in a nested study of exposures thought to cause recurrence and followed for up to 15 months. Weekly UV index values were obtained from the National Oceanic and Atmospheric Administration and matched to the participant's study center. We used marginal structural Cox models to account for potential confounding by measured time-varying psychological stress and contact use. Forty-four ocular HSV recurrences occurred, yielding an incidence of 4.3 per 1000 person weeks. The incidence of ocular HSV recurrence at 60 weeks for weeks where UV < 4 was 23% among participants who spent 0-7 hours outdoors and 26% for participants who spent 8+ hours outdoors. During weeks where UV 4+, the incidence of ocular HSV recurrence was 14% for those who spent 0-7 hours per week outdoors and 40% for those who spent 8+ hours per week outdoors. The weighted hazard ratios comparing those with 8+ hours of outdoor exposure to those with 0-7 were 0.84 (95% CI: 0.27, 2.63) and 3.10 (95% CI: 1.14, 8.48), for weeks with a UV index < 4, and 4+, respectively (P value for homogeneity = 0.19). We did not finely assess UV exposure with a dosimeter, and information about when participants spent their time outdoors was unavailable. However, HSV recurrences were observed prospectively and confirmed by study-certified physicians. Additionally, time updated reports reduced measurement error and allowed the use of modern methods to account for time-varying confounding. Eight or more hours per week spent outdoors was associated with an increased risk of ocular HSV recurrences only when UV index was 4+.

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THE DURATION OF EFFECTS OF ANTIBIOTIC EXPOSURES ON THE RISK OF CLOSTRIDIUM DIFFICILE INFECTION (CDI): A COHORT STUDY.

*Kevin Brown, David Fisman, Rahim Moineddin, Nick Daneman (University of Toronto, Toronto ON Canada)

The rising incidence of Clostridium difficile infection (CDI) could be lessened by reducing exposures to high risk antibiotics. However, the effect of reducing duration of exposure is less well understood. We sought to assess how the effects of antimicrobial exposures both cumulate over the course of antimicrobial therapy and abate after cessation. The source cohort consisted of all patients hospitalized at Sunnybrook Health Science Centre in the June 1, 2010 to May 31, 2012 period. Cases of CDI were identified prospectively, and their source of acquisition and timing of symptom onset were determined. Patient age, gender, procedures, and hospital pharmacy records were obtained from electronic hospital administrative records. Receipt of any antibiotic therapy was measured for each patient-day in a 30 day retrospective window. Cox proportional hazards regression was used while time-varying effects were modeled using distributed lag spline functions. Over the 24 month study period, a total of 47,241 patients were identified as having been admitted, of which 127 had new onset nosocomial CDI while hospitalized. The best fitting spline models suggested that the log-hazards was constant during antimicrobial therapy and that cessation of antibiotics was followed by an increase in risk for 2 days, which was subsequently followed by a rapid decline to zero over the next 12 days ($\chi 2$ 3df = 10.01, p = 0.02). After adjustment for age and hospitalization history, a 7 day antibiotic course was associated with 2-fold increase in average risk (hazard ratio = 1.96, 95% confidence interval: 1.32—2.92). This study yields insight into the etiology of CDI; our models suggest a possible exacerbation of risk in the 2 days following the end of antimicrobial therapy, which may be the first demonstration of this phenomenon in humans.

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A SOCIAL NETWORK INTERVENTION FOR REDUCING INFLUENZA-LIKE ILLNESS TRANSMISSION: THE EX-FLU CLUSTER RANDOMIZED TRIAL.

*Allison E Aiello, Erik Volz, Amanda M Simanek, Brian Davis, Erin Rees Clayton, Alison R Walsh, Kara Tarter, Jeanette Rainey, Charitha Gowda, Mychal Riley, Suzanne Ohmit, Arnold Monto, Arnold Monto (University of Michigan, School of Public Health, Department of Epidemiology, Center for Social Epidemiology and Population Health, Ann Arbor MI 48109)

The protective effects of voluntary isolation on influenza transmission have never been assessed in a randomized intervention study. We describe the design of the first year of a two-year randomized intervention aimed at reducing the spread of influenza among University students living in residence halls. Participants were randomly assigned by geographic cluster within residence halls to one of two sequestration protocols (3 day or 6 day) or control (no sequestration). All participants were instructed to report influenza-like illness (ILI) defined for this trial as cough and at least 1 other symptom: fever/feverishness, body aches or chills. Intervention group participants were instructed to begin their sequestration protocol immediately upon onset of ILI and compliance was assessed via weekly surveys. Control group participants were not instructed to participate in a sequestration protocol. A total of 547 individuals enrolled and 442 individuals provided data for analyses (186 in the 6-day group, 197 in the 3-day group, and 189 in the control group). There were 36 ILI reports; 2 from the 6-day group, 11 from the 3-day group, and 23 from the control group. The assortativity of ILI (i.e., tendency for an individual with ILI to be connected to others that have ILI) and the odds of reporting ILI according to the health status of identified contacts were calculated. Assortativity by ILI status was not statistically significant (0.3%) across the identified network. However, the odds of ILI was 3.2 times higher among those reporting at least one social contact with ILI versus no social contacts with ILI, controlling for cumulative number of contacts [OR = 3.22 (1.47, 7.04)]. Findings in year 1 of this study could reflect a mild influenza season and infectious contacts occurring outside of the identified social network. Year 2 studies are ongoing over a period of high influenza activity and should provide a larger number with ILI for future analyses.

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A MATHEMATICAL MODEL FOR HERD IMMUNITY AGAINST INFLUENZA IN LONG-TERM CARE FACILITIES IN NEW MEXICO.

*Aaron Wendelboe, Carl Grafe, Micah McCumber (University of Oklahoma Health Sciences Center, Oklahoma City OK 73104)

Introduction: The U.S. Centers for Disease Control and Prevention (CDC) recommends vaccinating health care workers (HCW) against influenza to achieve herd immunity to protect residents of long-term care facilities (LTCF). However, a previous mathematical model provided evidence that herd immunity cannot be achieved in LTCFs. We aimed to investigate the validity of these findings by developing a mathematical model for influenza using surveillance data from LTCFs in New Mexico. Methods: All 76 LTCFs in New Mexico were required to report influenza illnesses among residents and HCWs during influenza season 2006–07. Based on a previously published stochastic "Susceptible, Exposed, Infected, Removed" model of the transmission dynamics of LTCF residents, HCWs, and community visitors, we used monthly counts of influenza cases and proportions of vaccine coverage among residents and HCWs in all LTCFs to estimate each facility's influenza attack rates at HCW vaccination coverage levels from 0% to 100% by 10% increments. We used a mixed model to estimate the mean attack rates while controlling for clustering effects. A quadratic term was tested for curvilinear trend. We conducted sensitivity analyses to identify parameters affecting the herd immunity threshold. Results: The trend in attack rates by increasing HCW vaccination coverage was slightly curvilinear, with the quadratic term = -0.0018 (p = 0.027), indicating indirect protection induced by vaccination, but insufficiently strong to establish herd immunity. Small reductions (i.e., 2%) in the contact parameter of the community population had a large effect on the size of LTCF attack rates but not the curvilinear shape of the trend. Conclusions: LTCF administrators should continue to encourage all HCWs to get vaccinated annually against influenza. However, there is no threshold at which the need for vaccination ceases as our findings show that there is insufficient protection attributable to herd immunity.

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PREVALENCE OF H. PYLORI INFECTION IN A PORTUGUESE SAMPLE OF ADOLESCENTS. *Carlos Pereira, Nelio Veiga, Marco Baptista, Claudia Chaves, Paula Nelas, Odete Amaral, Manuela Ferreira, Jose Caldo, Santiago Teixeira (CI&DETS-Polytechnic Institute of Viseu; Health Science Department UCP; IPATIMUP FMUP; Group Schools Satao, Portugal)

Background: There are some gaps in knowledge of the prevalence and determinants of Helicobacter pylori (H. pylori) infection acquired during childhood. The aim of this study was to estimate the prevalence of H. pylori in a portuguese sample of adolescents using 13C-urea breath test (13C-UBT). Participants and Methods: A sample of 293 adolescents aged 12 to 18 years old, attending a public school in Satao, Portugal, was enrolled in this cross-sectional study. A self-administered questionnaire was answered by the adolescents in classroom in order to assess socio-demographic and symptoms. The adolescents were screened for H. pylori infection using the 13C-UBT test and needed to fast for at least one hour before the test. The 13C-UBT test consisted in the exhalation of carbon dioxide in samples before and after swallowing urea labeled with non-radioactive carbon-13. Prevalence was expressed in proportions and compared by the chi-square test. Crude odds ratio (OR) with 95% confidence intervals (CI) were used to measure the strength of association between H. pylori infection and the independent variables. Results: The prevalence of H. pylori infection was 40.4% (95% CI = 35.0-46.0). The H. pylori infection was associated with gender (female, OR = 1.52, 95% CI = 1.0-2.46), age (>15 years, OR = 1.78, 95% CI = 1.1-3.28) parents' educational level (>9th grade, OR = 1.53, 95% CI = 1.0-2.50), alcohol consumption (yes, OR = 1.45, 95% CI = 1.0-2.36), crowding index (≥1, OR = 3.49, 95% CI = 1.2-13.83), soft drink consumption (yes, OR = 0.48, 95% CI = 0.22-0.98). Conclusions: Nearly half of the adolescents were positive for H. pylori infection, suggesting that gastric pathology continues to be considered an important public health problem among the population, including among adolescents.

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MEDIATION BY STRUCTURAL EQUATION MODELING OR CAUSAL INFERENCE: WHAT IS THE DIFFERENCE? *Bianca De Stavola, Rhian Daniel, George Ploubidis, Nadia Micali (London School of Hygiene and Tropical Medicine, London England UK)

The study of mediation by path analysis, and more generally structural equation modelling, has a long tradition in the social sciences. However new insights from the causal inference literature have broadened its appeal, especially in health research. In this work we compare definitions, assumptions and estimation methods used in these two frameworks in order to highlight their commonalities and differences. We revisit how the controlled direct effect, and the natural direct and indirect effects defined in the causal inference literature can be estimated after fitting suitable structural equation models (SEM) and appropriately combining their parameters, extending previous work. Such estimation-by-combination is shown to be equivalent to estimation by parametric g-computation for certain models. These comparisons lead to clarifying the parametric identifying assumptions for these estimands when intermediate confounders are present, to relaxing certain non-confounding assumptions implicit in the SEM definitions, and to the implementation of simple sensitivity analyses. Simulated data are used to demonstrate the equivalences between the two approaches and data from a UK study of maternal pre-pregnancy BMI and risk of eating disorder behaviors in adolescent girls are analysed to illustrate the two approaches when studying the mediating effect of childhood growth. Our overall conclusions are that adopting the definitions of mediation parameters proposed in the causal inference literature leads to greater generality and explicit acknowledgement of the assumptions necessary for their identification, while appreciating when and how structural equation modeling is equivalent to parametric g-computation will lead to greater understanding by applied researchers of, and access to, causal inference methods.

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THE VALIDITY AND EFFICIENCY OF THE COMMON EFFECT TEST FOR SUBTYPE ANALYSIS IN CASE-CASE STUDIES. *Molin Wang, Aya Kuchiba (Channing Division of Network Medicine, Harvard Medical School, Departments of Biostatistics and Epidemiology, Harvard School of Public Health, Boston MA 02115)

To better understand the interplay between etiologic factors, cellular molecular characteristics, and disease evolution, "molecular pathology" and "epidemiology" have become integrated to generate the field of "Molecular Pathological Epidemiology (MPE)". MPE hypothesizes differential risks of exposure for different disease subtypes within a single disease entity. Hypothesis tests in MPE analyses can be categorized into two types of tests: subtype-specific tests, which assess an exposure effect on a particular disease subtype, and the common effect test, which compares the exposure effect across disease subtypes. MPE research can conducted using three different study designs: the prospective cohort, the case-control and the case-case. In this presentation, it will be shown that the common effect can be validly assessed in case-case studies by explicitly deriving the relationship between the relevant statistical models and their parameters in the three designs mentioned above. The efficiency of the common effect test in the case-case study will also be compared to that based on a case-control study, analytically and through simulation studies. Findings will be illustrated in a study of LINE-1 methylation sub-types of colon cancer in relation to alcohol intake.

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THE OPTIMAL METHOD FOR MEASURING SECONDHAND SMOKE EXPOSURE AMONG CHINESE PREGNANT WOMEN. *Chuanbo Xie, Xiaozhong Wen, Weiqing Chen, Peng Ding, Tao Liu, Yanhui He, Zhongzheng Niu, Xiaoying Wu, Shanyu Zhou, Jianmiao Lin, Xiaoling Guo (Department of Biostatistics and Epidemiology, School of Public Health, Sun Yat-Sen University, Guangzhou Guangdong China)

Objective: To combine maternal self-report and serum cotinine along with CYP2A6 genotypes to explore the optimal measurement for secondhand smoke (SHS) exposure during pregnancy. Methods: We analyzed the data from 545 Chinese pregnant women in Guangdong, Southern China. Pregnant women self-reported SHS exposure status and duration during pregnancy in hospital for delivery. PCR was used for CYP2A6*4 genotyping and ELISA for measuring serum cotinine. Area under receiver operating characteristic curve (AUROC) and Hosmer-Lemeshow test (H-L test) was used to assess the predictive ability of different SHS measures for small-for-gestational-age birth. Results: For self-report only, daily SHS exposure for 15 minutes or longer had higher predictive ability for risk of SGA (adjusted odds ratio [OR], 1.79 [95% confidence interval 1.08, 2.98]; AUROC, 0.639) than other SHS definitions based on ever exposure or weekly exposure for 15 minutes or longer (recommended by WHO). For serum cotinine only, the cut-off point 3 ng/ml had the highest predictive ability for risk of SGA (OR, 1.55 [1.02, 2.37]; AUROC, 0.645). For the combinations of self-report and serum cotinine, the definition of SHS exposure positive based on self-reported daily SHS exposure for 15 minutes or longer or serum cotinine 3 ng/ml or higher had highest predictive ability for risk of SGA (OR, 1.54 [1.01, 2.35]; AUROC, 0.648) than other possible combinations, including modified cut-off points of serum cotinine by CYP2A6 genotypes and serum cotinine 3 ng/ml or higher or CYP2A6*4 and self-reported daily SHS exposure for 15 minutes or longer. Predicted probability of SGA based on all candidate definitions of SHS exposure was similar to actual probability (H-L P-values greater than 0.05). Conclusion: In our sample, the combination of self-reported daily SHS exposure for 15 minutes and serum cotinine 3 ng/ml seemed to be the optimal measurement for SHS exposure during pregnancy.

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FROM EXPOSURES TO INTERVENTIONS: AN EXAMPLE IN PREGNANCY AND RESPONSE TO HIV THERAPY. *Daniel Westreich (Duke University, Durham NC 27705)

Typically, epidemiologic studies identify contrasts between an "always exposed" and a "never exposed" population. For example, we might ask about all-cause mortality if a given population were continuously exposed to smoking over five years, compared with that same population being completely unexposed to smoking during the same period. Such "exposure effects" are perhaps most valuable in discussing individual lifestyle changes, or in clinical care; they are somewhat less valuable in assessing what effect realistic public-health interventions might have in the population. For example, the answer to an "interventional" question such as "how many lives would be saved over five years under incentives which lead 20% of current smokers to quit smoking within one year, in this population?" is several steps removed from the always vs. never comparison. Various methods, among them population attributable fractions and generalized impact fractions, attempt to obtain more policy-relevant estimates of effect, but such methods often remain secondary in the epidemiologic literature; as well, methods for such interventional estimates have not been widely explored in longitudinal data. Here, we describe the use of the parametric g-formula as a tool for the estimation of population intervention effects in longitudinal data. Our discussion is motivated by a previous study of the effect of incident pregnancy on time to virologic failure among more than 7500 HIV-positive women initiating antiretroviral therapy in South Africa. We show that (i) interventional estimates of effect can be estimated straightforwardly using the parametric g-formula, and that (ii) exposure effects and population interventional effects can have dramatically different interpretations and magnitudes in real world data. Epidemiologists should consider estimating interventional effects instead of, or in addition to, exposure effects.

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A COMPARISON OF PROPENSITY SCORE AND MULTIVARIABLE ADJUSTMENT METHODS IN A REAL-WORLD COMPARATIVE EFFECTIVENESS STUDY OF GLAUCOMA TREATMENTS (RIGOR). *Jaclyn L. F Bosco, Kristina Franke, Anne L Coleman, Flora C Lum, Richard Gliklich, Zhaohui Su, Priscilla Velentgas (Quintiles Outcome, Cambridge MA 02139)

Evidence from analyses of simulated data suggests matching may be the preferred method for implementing propensity score (PS) adjustment in comparative effectiveness research, but whether this holds for real-world data is unknown. RiGOR is a prospective observational study conducted at U.S. ophthalmology practices that aims to compare the effectiveness of glaucoma treatments. We implemented multiple PS methods to estimate the association between initiating procedures versus medications with treatment success (≥15% reduction in intra-ocular pressure [IOP]) at 3-months among patients with clinically diagnosed glaucoma (N = 1697). A non-parsimonious PS model was built using stepwise selection ($p = 0.20$). Adjustment methods included multivariable regression, adjustment for continuous PS, trimming, stratification on PS quintile, and matching. Odds ratios (OR) and 95% confidence intervals (CI) were estimated for each PS method. Education, race/ethnicity, history of previous glaucoma procedures, glaucoma severity, and reason for change in glaucoma therapy differed by treatment type at baseline, but were balanced after matching. The association of treatment type with success at 3-months was similar when comparing crude (N = 1697, OR = 0.85; 95% CI = 0.70-1.03), multivariable adjusted (N = 1697; OR = 0.89; 95% CI = 0.70-1.13), trimmed N = 1646; OR = 0.82; 95% CI = 0.67-1.01), continuous PS adjusted (N = 1697; OR = 0.91; 95% CI = 0.73-1.13), stratified (N = 1697; OR = 0.92; 95% CI = 0.74-1.14), and PS matched (N = 1000; OR = 0.85; 95% CI = 0.66-1.09) methods. While PS matching improved covariate balance, 41% of patients were dropped from the analysis. Given the investment made by patients, physicians, researchers, and funders to collect prospective observational study data, methods to control for confounding that do not require dropping large numbers of patients from analysis as with PS matching are preferred when they yield equivalent results.

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COMPARISON AND META-ANALYSIS OF RESULTS FROM RANDOMIZED AND NON-RANDOMIZED STUDIES IN EPIDEMIOLOGIC RESEARCH. *Elizabeth Yanik, Alan Brookhart, Til Sturmer, Charles Poole (University of North Carolina at Chapel Hill, Chapel Hill NC 27599)

Background: Previous reviews and meta-analyses have come to mixed conclusions about the degree of concordance between results from randomized studies (RCTs) and non-randomized studies (nRCTs). Methods: We systematically identified meta-analyses and systematic reviews that compared RCTs and nRCTs for at least 3 different exposure-outcome associations in a peer-reviewed journal through a search of the PubMed database. Relative effect estimates and standard errors for RCTs and nRCTs were abstracted for each exposure-outcome association. Relative odds ratios (RORs) were calculated as the ratio of the nRCT estimate divided by the RCT estimate, where effect estimates were always coded so that the nRCT estimate would be ≥1. Results: We identified twelve papers published between 2000-2011 for inclusion. These papers included 207 unique associations, including 140 evaluating a treatment intervention, 62 a prevention intervention, and 5 a treatment and prevention intervention. Over all the associations evaluated, the median ROR was 1.12 with an interquartile range of 0.84-1.70, and a total range of 0.2-24. The nRCT estimate and RCT estimate were on opposite sides of the null for 25% of associations. Among the associations in which the RCT and nRCT estimates were on the same side of the null, 46% had an ROR greater than 1, indicating an nRCT estimate further away from the null than the RCT estimate. For 16% of associations RORs indicated the RCT estimate was statistically significantly different from the nRCT estimate with an alpha of 0.05. In 9% of the comparisons the ROR estimate was statistically significant and the RCT and nRCT estimates were on opposite sides of the null. Conclusion: Across all comparisons, the extent of agreement between RCT results and nRCT results varied widely. However, the majority of comparisons showed similar RCT and nRCT estimates, with only a small percentage indicating meaningfully different results between the two study types.

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COMPARISON OF G-METHODS TO CONTROL TIME-VARYING CONFOUNDING IN A COHORT OF BONE MARROW TRANSPLANT PATIENTS. *Alexander Keil, Jessie Edwards, Ashley Naimi (University of North Carolina, Chapel Hill NC 27514)

Graft-versus-Host-Disease (GvHD) is a potentially serious side-effect of bone marrow transplant (BMT) among leukemia patients. However, GvHD can also occur as part of a robust immune recovery and positive prognostic indicator. Estimation of the effect of GvHD on mortality is complicated by time-varying confounding by platelet count and leukemia relapse. G-methods can appropriately address time-varying confounding and should be used to estimate the GvHD-mortality relation. The choice between g-methods should be driven by causal knowledge. But in the absence of such knowledge choice of methods is unclear. We compare three g-methods to estimate the effect of GvHD on mortality in a cohort of 137 leukemia patients followed from BMT to death or administrative censoring at 5 years: a marginal structural Cox proportional hazards model, a structural nested failure time model, and parametric g-computation. Using these methods we estimated the hazard ratio, median mortality-time ratio, and cumulative incidence ratio for the effect of GvHD on mortality, and compare the results across each method. We also use Monte Carlo simulations to compare methods when the true exposure-response relationship is known. During follow up, 73 (53%) of the patients developed GvHD, 42 (31%) experienced relapse, and 120 (88%) experienced a return to normal platelet levels. Hazard ratios (HR) marginal structural models (HR = 1.18), structural nested failure time models (HR = 1.20), and the parametric g-formula (HR = 1.80) indicated that GvHD is associated with a slight increase in mortality, which was lower than a standard Cox model that inappropriately adjusted for time-varying confounders (HR = 2.36). Time ratios and cumulative incidence ratios followed similar patterns. Simulations suggest that, when the correct causal model is known and fits assumptions from all three methods, that parametric g-computation yields the lowest mean squared error of the three models. These results suggest that parametric g-computation should be used when the causal model is known, and we will compare methods under model misspecification.

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UNDERSTANDING THE CONTRIBUTION OF ENVIRONMENTAL EXPOSURES TO SCHOLASTIC ACHIEVEMENT. *Sheryl Magzamen, Pamela Imm, Michael Amato, Colleen F Moore, Marty S Kanarek (University of Oklahoma Health Sciences Center, Oklahoma City OK 73102)

Regression techniques that estimate mean effects, such as traditional ordinary least squares (OLS) regression, may mask important information that is contained in the tails of the distribution of the outcome. Further, if there is more than one single slope that can describe the relation between a response variable and predictor variable, basic assumptions that underlie OLS are violated. Quantile regression (QR) is a technique that can estimate multiple rates of change from the minimum to the maximum value of a response variable. We implemented quantile regression analysis to understand the relation between early childhood lead exposure and performance on end of grade standardized tests in the Wisconsin Childhood Lead Levels and Educational Outcomes (CLLEO) Study. A total of 1,109 students who were tested for blood lead levels (BLL) before age three consented to have results from the 4th grade Wisconsin Knowledge and Concepts Exam (WKCE) provided to the study. Children were considered exposed if 10mcg $\leq$BLL $\leq$19mcg and unexposed if BLL < 5mcg. Exposure, race/ethnicity, parent-rated child health, and parent level of education were included as explanatory variables in a model with scaled scores on the reading portion of the 4th grade WKCE. QR models were estimated at 0.05 increments from 0.05 to 0.95. In OLS regression, lead exposure was associated with a 16.19 point decrease in reading scores (95% CI: -22.5, -9.9). In QR regression, lead exposure was associated with a 37 point decrease in reading scores (95% CI: -82.0, -2.4) at the 0.05 quantile, and at the 0.85 quantile, lead exposure was associated with an 11 point decrease in reading scores (95% CI: -21.6, -0.2). Race, parental education and child's health status had fairly consistent relationships with reading scores across the distribution. Estimates commonly derived from traditional regression techniques may not adequately address health outcome and exposure disparities, particularly for groups with outcome values on the tail ends of a distribution.

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RECENT DEVELOPMENTS IN CAUSAL MEDIATION ANALYSIS WITH MULTIPLE MEDIATORS: BRIDGING THEORY AND PRACTICE. *Rhian Daniel, Bianca De Stavola (London School of Hygiene and Tropical Medicine, London United Kingdom)

Epidemiologic analyses often attempt to decompose the effect of an exposure on an outcome into its effect via a number of different pathways. For example, the effect of heavy alcohol consumption on systolic blood pressure (SBP) may be separated into an effect via body mass index (BMI), an effect via the liver enzyme gamma-glutamyl transpeptidase (GGT), an effect via both BMI and GGT, and an effect via other pathways (not through BMI or GGT) - often called the direct effect. Much progress has been made, mainly due to contributions from the field of causal inference, in understanding the precise nature of estimands that capture these sorts of effects, the assumptions under which they can be identified from data, and statistical estimation methods for doing so. However, the focus in the causal inference literature has been mostly on the decomposition of an effect around and through a single mediator, or a set of mediators considered en bloc, hence the two components: a direct and an indirect effect. In this talk we describe novel, counterfactually-defined path-specific effects that permit the decomposition of the total effect of an exposure on an outcome into a sum of numerous path-specific effects through many mediators, where the mediators are permitted to have a causal effect on each other. We show that there are many ways in which this decomposition can be done, discuss the strong structural and modelling assumptions under which the effects can be estimated, together with a sensitivity analysis approach when a particular subset of the assumptions cannot be justified. Illustrating these ideas using a data on alcohol consumption, SBP, BMI and GGT from the Izhevsk Family Study, we focus on the ambitious nature of multiple mediation analyses, giving some practical guidance on how progress can be made.

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EVIDENCE OF FREE SAMPLE USE AMONG NEW USERS OF BRANDED STATINS: IMPLICATIONS FOR PHARMACO- EPIDEMIOLOGY. *Xiaojuan Li, M Alan Brookhart (Department of Epidemiology, UNC Gillings School of Global Public Health, Chapel Hill NC 27599)

Incomplete capture of prescription medication use by healthcare claims databases can occur when patients use free sample drugs, which could result in drug exposure misclassification and adversely affect research and quality improvement activities that rely on these data. To assess the extent of free sample use, the authors examined the low-density lipoprotein (LDL) test results recorded before the first filled prescription claim among a cohort of 60,934 new users of statins using MarketScan Databases, 2007-2010. LDL lab values were analyzed using a two-component Gaussian mixture model to estimate the proportion of patients filling a new prescription may already be on treatment. Among patients filling a branded statin, LDL values were bimodal, consisting of two Gaussian distributions: one, which made up 16.6% of the population, had much lower LDL values (mean = 73.0 mg/dL, standard deviation [SD] = 18.0 mg/dL) compared to the second (mean = 139.3 mg/dL, SD = 41.2 mg/dL), suggesting drug use prior to first prescription claim. Among patients filling a generic statin, LDL levels were substantially higher with no evidence of bimodality that would suggest prior sample use. Further analyses on a more restricted cohort of patients with at least two sequential LDL labs before filling a statin prescription (n = 10,617) showed similar results for the last LDL (branded drug: mean = 76.0 mg/dL, SD = 18.4 mg/dL; mean = 132.9 mg/dL, SD = 39.3 mg/dL) but the proportion was 27.5% for the distribution of lower LDL values. The last LDLs among generic users did not show evidence of bimodality that would suggest prior sample use. This study contributes compelling evidence that exposure misclassification due to free sample utilization does exist when using pharmacy claims data to define exposure status. Future research is needed to examine approaches that can be used to better ascertain true incident medication use, particularly in comparative studies of medications.

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USE OF MARGINAL STRUCTURAL MODELS ACCOUNTING FOR COMPLEX EXPOSURE HISTORY IN ASSESSING THE EFFECT OF PREGNANCY ON ADHERENCE TO HAART. *Cassidy Henegar, Mhairi Maskew, Daniel Westreich (University of North Carolina, Chapel Hill NC 27599)

Standard methods for construction of inverse probability weights used to adjust for confounders in marginal structural models do not account for multiple changes in exposure status during the period of follow-up. We wished to estimate the effect of pregnancy and the postpartum period (six months following pregnancy) on adherence to HAART (highly active antiretroviral therapy) among women established on treatment in Johannesburg, South Africa. In this cohort of 7,534 women, 918 experienced pregnancy after treatment initiation. We applied a novel weighting structure incorporating the exposure transitions occurring in this cohort: not pregnant to pregnant (experienced by some women) and pregnant to postpartum (experienced by all women among those that become pregnant, and by no women who did not become pregnant). For comparison, we also used a more-typical approach to weight construction, collapsing pregnancy and the postpartum into a single exposure category. Adherence was defined as having 100% pill coverage between prescription refills. Standard weighting for our marginal structural log-binomial regression models indicated no effect of pregnancy on adherence to HAART (Risk Ratio: 1.17, 95% Confidence Interval: 0.88, 1.56). Using the alternative weighting structure to account for all three exposure categories, pregnancy remained unassociated with adherence (RR: 0.97, 95% CI: 0.64, 1.48), but risk of non-adherence increased markedly during the postpartum period (RR: 1.68, 95% CI: 1.10, 2.58). Marginal structural models constructed with inverse probability weights allowing for multiple changes in exposure status were able to identify a period of increased risk of non-adherence, the postpartum period, that was not observed using a standard weighting approach.

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USE OF BOX-COX POWER EXPONENTIAL AND BOX-COX-COLE-GREEN DISTRIBUTIONS TO GENERATE STANDARD NORMAL SCORES ON THE BAYLEY SCALES OF INFANT DEVELOPMENT-III FOR A COHORT OF MALAWIAN CHILDREN. *Elizabeth Cromwell, Stephen Cole, Anna Dow, Queen Dube, Annelies Van Rie (University of North Carolina Chapel Hill, Chapel Hill NC 27599)

The Bayley Scales of Infant Development-III (BSID-III) measures cognitive, fine motor (FM), gross motor (GM), expressive communication (EC) and receptive communication (RC) development in children age 1-42 months. To compare scores across ages, the raw score is converted to a scaled score based on norms derived from a sample of United States (US) children. The scaled scores classify children as having normal (score within one standard deviation (SD) of the mean scaled score), mildly delayed (-2 SD < score < -1 SD) or severely delayed (score < -2 SD) development. The BSID-III is also used in international settings even though US scores may introduce outcome misclassification as the raw score distribution in the US normative sample may differ from that in other populations due to cultural and environmental influences. We used a sample of healthy Malawian children to construct BSID-III norms appropriate for Malawi. Norms were generated using the Box-Cox Power Exponential (BCPE) and Box-Cox-Cole-Green (BCCG) distributions, which accommodate skewed data and a continuous predictor to generate normative curves. The BCPE distribution is characterized by a power transformation of the response variable and is described by four parameters that relate to the median, variance, skewness, and kurtosis; the BCCG distribution includes these parameters except kurtosis. A non-parametric function of age modeling these parameters is used to generate smooth age-specific centile curves for BSID-III. The percentiles were used to convert raw scores into standard z-scores, allowing classification of normal, mild or severely delayed development according to the Malawian norms. Weighted kappas for agreement between US and Malawian norms were as follows: 0.47 for cognitive; 0.52 for FM; 0.62 for GM; 0.57 for EC; and 0.49 for RC. We compare the study results to determine the potential bias introduced by US norms.

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SUBJECTIVE SOCIAL STATUS: RELIABILITY OF THE MACARTHUR SCALE IN BRAZILIAN LONGITUDINAL STUDY OF ADULT HEALTH (ELSA-BRASIL). *Luana Giatti, Lidyane Camelo, Josi Rodrigues (Universidade Federal de Ouro Preto, Ouro Preto Minas Gerais Brazil)

Background: The MacArthur Scale of Subjective Social Status intends to measure the subjective social status using a numbered two stepladder image (society and community). This study investigated the reliability of the MacArthur scale in a subsample of the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). Because the ELSA-Brasil study is an occupational cohort, we also created a ladder to assess how participants perceive themselves in the occupational hierarchy (work related ladder) that was included in this analysis. Furthermore, it investigated whether the test- retest reliability of the scales differ according to age, sex and schooling. Methods: Three scales were employed using different references: 1) the overall socioeconomic position; 2) the socioeconomic situation of the participant's closer community; 3) the workplace as a whole. A total of 245 of the ELSA participants from six different states were involved. They were interviewed twice by the same person within an interval of seven to fourteen days. The reliability of the scale was assessed with weighted Kappa statistics and intraclass correlation coefficient (ICC), with their respective 95% confidence interval (CI). Results: Kappa values were 0.62(0.58 to 0.64) for the society ladder; 0.58(0.56 to 0.61) for the community-related ladder; and 0.67(0.66 to 0.72) for the work-related ladder. The ICC ranged from 0.75 for the work ladder to 0.64 for the community ladder. These values differed slightly according to the participants' age, sex and education category. Conclusions: The three ladders showed good stability in the test-retest, except the community ladder that showed moderate stability. Because the social structure in Brazil is rapidly changing, future qualitative and longitudinal studies are needed to confirm and understand the construct underlying the MacArthur Scale in Brazil.

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BROADENING THE CASE DEFINITION OF GULF WAR ILLNESS OBSCURES RESEARCH FINDINGS: DIRE IMPLICATIONS OF THE NEW IOM RECOMMENDATION. *Robert Haley (University of Texas Southwestern Medical Center, Dallas TX 75390)

Presently 2 case definitions of Gulf War illness are widely used in epidemiologic research: 1) the Factor definition, a narrow one derived by factor analysis of typical symptoms, and 2) the Chronic Multisymptom Illness (CMI) definition, a broad one requiring only 2 symptoms, 1 from 2 of 3 symptom domains. The Institute of Medicine (IOM) recently recommended further broadening the case definition. We evaluated the impact of broadening the definition by comparing key research findings in zones of the Venn diagram of the overlap of the 2 definitions in a nationally representative nested case-control sample (N = 2,095), containing a survey measure of exposure to low-level sarin nerve gas (heard nerve gas alarms) and the genotype of the PON1 Q192R polymorphism and the serum activities of its Q and R isoenzymes. The Q isoenzyme is the body's main defense barrier against low-level sarin exposure. The Factor definition was almost entirely contained within the broader CMI, but the CMI contained an area outside the Factor circle of about equal magnitude. Controlling for multiple covariates and a propensity score, the gene-environment interaction was strong when calculated with the cases in common on the Factor and CMI definitions [relative excess risk of interaction (RERI) 5.59 (2.15-12.71), attributable proportion (AP) 0.62 (0.30-0.78), synergy index (S) 3.350 (1.53-7.38)], but it was far weaker when calculated with the cases defined by the full CMI definition [RERI 2.20 (0.49 - 4.37), AP 0.47 (0.11 - 0.67), S 2.63 (1.14 - 6.07)]. In the zone of the Venn diagram in the CMI but not the Factor definition, there was no evidence for the interaction [RERI 0.58 (-0.98 - 2.40), AP 0.23 (-0.52 - 0.58), S 1.62 (0.46 - 5.72)]. Thus, broadening the Factor definition to the larger CMI definition reduced its power to detect the interaction. Further broadening the case definition will further reduce its usefulness for research.

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ADAPTIVE PAIR-MATCHING IN THE SEARCH TRIAL: CONSEQUENCES FOR DESIGN EFFICIENCY, ESTIMATION AND INFERENCE. *Laura Balzer, Maya Petersen, Mark van der Laan (University of California, Berkeley, Berkeley CA 94720)

The Sustainable East Africa Research in Community Health (SEARCH) study is a large community randomized trial, which aims to estimate the effect of targeted testing and streamlined antiretroviral therapy at all CD4 levels on HIV incidence in rural East Africa. Considering the limited number of communities, concerns for study validity, and potential gains in efficiency, the SEARCH consortium has pair-matched communities on important determinants of the HIV epidemic. Specifically, 32 communities were sampled from the target population. Then using the baseline characteristics of all communities, the best 16 matched pairs were selected and the intervention randomized within the pairs. As a consequence of this *adaptive pair-matched design*, the treatment assignment depends on the baseline covariates of all communities sampled. Thereby, the observed data cannot be considered as 16 independent, identically distributed (i.i.d.) pairs of units, as current practice assumes. Instead, the observed data consist of 32 dependent communities. As detailed in van der Laan, et al. "Adaptive matching in randomized trials and observational studies" *Journ. Stat. Res.*: in press, we explored the implications of this design. Contrary to classic pair-matched trials, adaptive pair-matching does not risk reducing design efficiency and is expected to increase study power under plausible assumptions. Targeted minimum loss-based estimation (TMLE) can be implemented as if the data were from a completely randomized trial and by making use of covariate data will be more efficient than standard estimation approaches. Inference for the TMLE can be based on the normal distribution with variance given by the variance in the completely randomized design minus the covariance of residuals within matched pairs. Our theoretical results are supported by simulations and demonstrate that adaptive pair-matching protects the validity of the randomized trials while reducing estimator variance.

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ASSOCIATIONS BETWEEN INSUFFICIENT SLEEP, HEALTH-RELATED QUALITY OF LIFE, AND LIFE SATISFACTION, AMONG ADULTS WITH ASTHMA: A MEDIATION MODEL APPROACH. *Lauren Drinkard, Vinay Cheruvu (Kent State University College of Public Health, Kent OH 44242)

Abnormalities of sleep in adults with asthma may have adverse effects on Health-Related Quality of Life (HRQOL) and can result in reduced life satisfaction. The purpose of this research was to examine the effect of insufficient sleep on life dissatisfaction in adults with asthma and to determine if HRQOL indicators mediate the effect. Cross-sectional data from the 2010 Behavioral Risk Factor Surveillance System (BRFSS) involving adults with asthma were used for this study (n = 36,913). Perceived insufficient sleep, the primary exposure of interest, was assessed asking the question "During the past 30 days, for about how many days have you felt you did not get enough rest or sleep?" and was categorized into two groups (<14 days vs. 14 days). HRQOL constructs measuring poor "self-rated health", "physical health", "mental health", & "social functioning" (past 30 days) were the mediators of interest and each was categorized into two groups (<14 days vs. 14 days). Perceived satisfaction with life, the outcome of interest, was categorized into two groups (satisfaction vs. dissatisfaction). Logistic regression models were used to examine if insufficient sleep was directly associated with life dissatisfaction and if HRQOL indicators mediate the relationship, adjusting for all potential confounders. Data were analyzed in 2012 and accounted for complex sampling design of the BRFSS. HQROL significantly mediated the effect of insufficient sleep on life dissatisfaction. The proportion of effect mediated by Mental Health was 44%, followed by Poor Health (34.5%), General Health (25.5%), and Physical Health (24.6%). Mediation remained significant after adjusting for potential confounders. These results provide new evidence that HRQOL mediates the relationship between insufficient sleep and reduced life satisfaction. Public health practitioners should be aware of sleep quantity and quality as they have implications for health outcomes in adults with asthma.

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SEAFOOD CONSUMPTION AMONG PREGNANT WOMEN AND NON-PREGNANT WOMEN OF CHILDBEARING AGE IN THE UNITED STATES, NHANES 1999-2010. *Hilda Razzaghi, Sarah Tinker (Center for Disease Control and Prevention, Atlanta GA 30333)

Background: Long-chain polyunsaturated fatty acids found in seafood are essential for optimal neurodevelopment of the fetus. However, concerns about mercury contamination of seafood and its potential harm to the developing fetus have created uncertainty about seafood consumption for pregnant women. Purpose: We compared fish and shellfish consumption patterns, as well as their predictors, among pregnant and non-pregnant women of childbearing age in the U.S. Methods: Data from 1,260 pregnant women aged 16-49 years from the 1999-2006 National Health and Nutrition Examination Survey (NHANES), and 8,210 non-pregnant women aged 16-49 years from the 1999-2010 NHANES were analyzed. Frequency and type of seafood consumed and adjusted associations of multiple characteristics with seafood consumption were estimated for pregnant and non-pregnant women, separately. Time trends were also examined. Results: There were no significant differences in the prevalence of fish or shellfish consumption, separately or combined, between pregnant and non-pregnant women. Seafood consumption was associated with increasing age, higher poverty income ratio, and higher education among pregnant and non-pregnant women, and among fish consumers these groups were more likely to consume ≥3 servings in the past 30 days. Tuna and shrimp were the most frequently reported fish and shellfish, respectively, among both pregnant and non-pregnant women. We observed no time trends. Conclusion: There were few differences in seafood consumption between pregnant and non-pregnant women, and the factors related to seafood consumption were similar for both groups. Our data suggest that many women are not consuming the recommended amount of seafood.

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THE METHYLMALONIC ACID (MMA) CONCENTRATION OVERESTIMATES THE PREVALENCE OF VITAMIN B12 DEFICIENCY IN SENIORS. *Martha Savaria Morris, Paul F Jacques, Jacob Selhub (Jean Mayer United States Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, Boston MA 02111)

Estimates of the burden of vitamin B12 deficiency in seniors have risen from ≈1% in 1960 to 5% in the 1990s and up to 20% by 2000. This trend is due to secular changes in the markers used. Specifically, megaloblastic anemia and plasma B12 < 148pmol/L are rare, and signs of low B12 function, like high MMA, common. We recently found enhanced 8-y cognitive decline in Framingham Heart Study (FHS) subjects with plasma B12 below the 40th%-ile or MMA > 221nmol/L, the 60th%-ile. The 2 assays disagreed 35% of the time – perhaps due to limitations of the B12 assay – but treating MMA as the gold standard is controversial. In the present study, we assessed associations with cognitive function and decline to test each marker's performance. Among 260 FHS subjects, Mini-Mental State Examination scores of the 16% who were in the worst 40% of the distribution for both assays declined significantly more ($\beta = -0.49$; 95% confidence interval [CI]: -0.38, -0.6) than those of subjects in the best 60% for both assays ($\beta = -0.18$; 95% CI: -0.24, -0.12) after control for age, education, plasma folate, and creatinine, but decline was not enhanced in strata with isolated low B12 ($\beta = -0.11$; 95% CI: -0.23, 0.01) or high MMA ($\beta = -0.22$; 95% CI: -0.31, -0.13). In similar NHANES (1999-2002, n = 2059) analyses, 377 seniors with MMA > 221nmol/L had lower Digit Symbol Substitution Test (DSST) scores than 1682 with lower MMA ($\beta = -2.7$; 95% CI: -4.8, -0.69; P = 0.01). However, that result was driven by a minority with both high MMA and B12 < 170pmol/L (n = 72), who scored far worse than 1631 subjects with neither risk factor ($\beta = -6.5$; 95% CI: -10.2, -2.1). The 305 seniors with high MMA and serum B12 ≥ 170pmol/L did not differ from those referents ($\beta = -1.9$; 95% CI: -4.4, 0.61; P = 0.137), nor did the 51 with low B12 alone ($\beta = -0.27$; 95% CI: -5.5, 5.0), despite a large disparity between all subjects with B12 < 170pmol/L and the rest ($\beta = -3.6$; 95% CI: -7.1, -0.22). B12 status is best assessed using a combination of markers.

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RACIAL/ETHNIC DIFFERENCES IN DIETARY PATTERNS IN ADOLESCENTS: FINDINGS FROM EAT 2010. *Gretchen Cutler, Peter Hannan, Nicole Larson, Dianne Neumark-Sztainer (Medica Research Institute, Minnetonka, MN 55305)

The objective of this study was to identify similarities and differences in dietary patterns by race/ethnicity in a diverse adolescent cohort. The EAT 2010 (Eating and Activity in Teens) study collected surveys and food frequency questionnaires from 2540 students (54% female) in 20 public schools in Minneapolis/St. Paul, Minnesota during the 2009-2010 academic year. The racial/ethnic backgrounds of the participants were as follows: 20% white, 28% black, 20% Asian American, 17% Hispanic, 15% mixed/other. Usual dietary intake was assessed using the previously validated, semi-quantitative Youth and Adolescent Food Frequency Questionnaire and dietary patterns were identified using factor analysis. In all racial/ethnic groups "fruit" and "vegetable" patterns were identified along with a "sweets" pattern (loading highly on foods including brownies, cake, and candy). Other identified patterns were not similar across all groups: a "fast food" pattern (hamburgers, French fries) was identified in white, Hispanic and Asian American adolescents; a "meals at home" pattern (macaroni and cheese, grilled cheese, French toast) was identified in black, Hispanic, Asian American, and mixed/other adolescents; a "healthy meals" pattern (tofu, grains, vegetables, dark bread) was identified in white adolescents. This study found similarities and differences in dietary patterns in adolescents with different racial/ethnic backgrounds. An important next step is to study predictors of dietary patterns as this type of information can be used to develop and target interventions aimed at improving dietary intake among different groups of adolescents.

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DIETARY TOTAL PROTEIN RELATED TO CANCER MORTALITY AND CANCERS OF DIGESTIVE ORGANS MORTALITY IN BANGLADESHI ADULTS: THE HEALTH EFFECTS OF ARSENIC LONGITUDINAL STUDY (HEALS). *Maria Argos, Stephanie Melkonian, Faruque Parvez, Mohammad Rakibuz-Zaman, Alauddin Ahmed, Yu Chen, Habibul Ahsan (The University of Chicago, Chicago IL 60637)

Background: The effect of dietary composition on mortality in Bangladesh and other low-income countries is largely unknown. Objective: We examined whether percentages of dietary energy derived from total protein and total fat were associated with all-cause and cancer mortalities in a Bangladeshi population. Methods: Participants were from the Health Effects of Arsenic Longitudinal Study (HEALS) cohort. Percentages of dietary energy derived from total protein and total fat were assessed using a validated food-frequency questionnaire. Results: Percentage of dietary energy from protein appeared to be significantly associated with cancer mortality. Fully adjusted hazard ratios for cancer mortality in increasing tertiles of percentage of dietary energy from protein were 1.0 (reference), 1.14 (0.68, 1.91), and 1.81 (1.05, 3.11) (P for trend = 0.028). Additionally, the associations were particularly strong when analyses were restricted to deaths from cancers of the digestive organs. Fully adjusted hazard ratios for digestive organ cancer mortality in increasing tertiles of percentage of dietary energy from protein were 1.0 (reference), 2.24 (0.90, 5.58), and 4.79 (1.86, 12.34) (P for trend = 0.001). No significant associations in relation to mortality were observed for percentage of dietary energy from fat. Conclusion: Our findings show percentage of dietary energy from protein is an important risk factor or proxy to an important risk factor for cancer mortality in a rural Bangladeshi population.

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AN IMPROVED STATISTICAL METHOD TO ESTIMATE USUAL INTAKE DISTRIBUTION OF NUTRIENTS BY AGE GROUP. *Hiroshi Yokomichi, Tetsuji Yokoyama, Kuniko Takahashi, Nobuo Yoshiike, Zentaro Yamagata, Toshiro Tango (University of Yamanashi, Chuo Yamanashi Japan)

The distribution of usual intake of nutrients in a given population is one of the major concerns in public health nutrition and is used to assess and prevent nutritional problems. The distribution of usual intake cannot be measured directly, but can be estimated from a dietary survey that spans multiple days. The prevalence of nutritionally high-risk people, defined as the proportion of a population that does not achieve the dietary reference intake (DRI), can be estimated from the distribution of usual intake in the population. Although several methods have been proposed, there is no universally accepted method for estimating the distribution and prevalence of nutritionally high-risk people. Nusser et al. proposed a semi-parametric model and developed software that is commonly used to accomplish this estimation; their model is known as the Iowa State University (ISU) method. Although Nusser's method is available to dietitians, one problem still remains. It is often the case that the usual intake distribution needs to be estimated for subgroups such as sex and age groups. Waijers et al. proposed another parametric model based on a mixed-effect model to resolve this issue. Waijers's model assumes that the mean structure of usual intake varies depending on the subject's age and this model is useful when the usual intake of a nutrient is justifiably assumed to vary with age. However, Waijers's model assumes a constant between-subject variance and a constant within-subject variance of nutritional intakes for different ages: this is problematic because this assumption is not always correct. In this study, we built a mixed-effect model with changing variance depending on the subject's age to enable nutritional intake modeling that fits better with actual data. We used simulation studies to compare the performance of the new method with that of 2 previously proposed methods. Our proposed method outperformed them, particularly in a realistic situation and with a small sample size, providing a more accurate and precise estimate of the prevalence of nutritionally high-risk people. This method will help promote the use of DRIs, help improve our understanding of the nutritional status among populations, and aid in confronting the challenges of public health nutrition.

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OMEGA-3 FATTY ACIDS AND RHEUMATOID ARTHRITIS-RELATED AUTOANTIBODIES IN A POPULATION AT INCREASED RISK FOR RHEUMATOID ARTHRITIS. *Ryan W Gan, Kendra A Young, M Kristen Demoruelle, Kevin D Deane, V Michael Holers, Jill M Norris (University of Colorado, Denver, Aurora CO 80045)

Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by systemic inflammation and circulating autoantibodies (Ab), which can be present years prior to RA diagnosis, and may define preclinical disease. Evidence suggests intake of anti-inflammatory omega-3 (n-3) fatty acids may decrease severity of RA. The role n-3 fatty acids play prior to disease onset is unknown. Methods: The Studies of the Etiology of RA (SERA) is a multisite cohort study following RA-free first-degree relatives of RA probands (FDRs) at-risk for future RA. We used a nested case-control design, with 40 cases positive (+) for a high risk Ab profile (HRP) (ie, + for ≥2 rheumatoid factor isotypes or + for anti-cyclic citrullinated peptide (CCP) Ab) on ≥2 visits, and 34 controls always negative for Ab, frequency matched on sex and study site. As a biomarker of fatty acid status and intake, n-3 fatty acid levels were measured in stored red blood cell (RBC) membranes, obtained from a single visit, and analyzed using multivariable linear regression. Results: No differences in total n-3 fatty acids were observed between HRP cases and controls, adjusting for shared epitope (≥1 HLA-DRB1 allele) and race (non-Hispanic white vs. other). We then limited our cases to the 16 who were CCP + , which is >98% specific for RA. CCP+ cases had lower total n-3 fatty acids than controls (53.1 vs. 60.6 μg/mL, p = 0.03), adjusting for race. Case-control differences persisted for marine n-3 fatty acids (summed eicosapentaenoic acid and docosahexaenoic acid) (31.8 vs. 37.9 μg/mL, p = 0.03), but not for the non-marine n-3 alpha-linolenic acid (p = 0.80). Conclusion: Lower marine n-3 fatty acid status may be associated with highly-specific RA-related autoimmunity in FDRs without RA, offering preliminary evidence n-3 fatty acids may be protective of preclinical autoimmunity. Additional CCP+ cases and controls were selected for confirmation.

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LOW DOCOSAHEXAENOIC ACID (DHA) INTAKE AND SIGNIFICANT MATERNAL DHA DEPLETION IN THE 3RD TRIMESTER OF PREGNANCY. *Jin-Ping Zhao, Emile Levy, Bryna Shatenstein, Pierre Julien, Anne Monique Nuyt, Lin Xiao, Schohraya Spahis, Alain Montoudis, William D Fraser, Zhong-Cheng Luo (CHU Sainte-Justine, University of Montreal, Montreal Canada)

Docosahexaenoic acid (DHA; C22:6n-3) is important for fetal brain growth and development. In particular, the 3rd trimester of pregnancy is a period of rapid fetal brain growth. There is a relative lack of data on the profile and ontogeny in circulating DHA in the 3rd trimester of pregnancy. Fetus depends on the mother for DHA that is obtained from her diet or endogenously converted from a-linolenic acid (C18:3n3). The conversion rate is up-regulated by pregnancy, but may be down-regulated by conditions such as gestational diabetes and high level of linoleic acid (LA; C18:2n6, gt3.0% of energy) in the diet. In a singleton pregnancy cohort (n = 307) study in Montreal, Canada, we investigated the alterations in plasma fatty acids concentraions during the 3rd trimester of pregnancy between 24-28 weeks and 32-35 weeks gestation, and the effects of food intakes based on a food frequency questionnaire administered at 24-28 weeks gestation. The median intake of DHA was ~100 mg/day, and not significantly different between gestational diabetic (n = 210) and non-diabetic (n = 21) women (P = 0.5). More than 90% of women had DHA intake below the recommended intake of 300 mg/day. Plasma DHA levels decreased by more than 10% from 24-28 weeks (mean ± SD: 1.9 ± 0.5%) to 32-35 weeks (1.7 ± 0.5%) gestation (P < 0.0001). Dietary intake of DHA at 24-28 weeks was positively correlated with plasma DHA levels at 24-28 and 32-35 weeks (gt0.38, P < 0.0001). The mean intake of LA was high (11.3 ± 4.3 g/day, ~5.0% of energy). The results suggest that maternal DHA depletion is significant in the 3rd trimester of pregnancy. Low and inadequate DHA, high LA intake is extremely prevalent in this study population. DHA supplementation and decreased intake of LA-riched foods in pregnancy should be advocated to promote healthy fetal development.

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RELATION OF DIETARY FAT INTAKE TO PERIPHERAL LEUKOCYTE TELOMERE LENGTH IN POSTMENOPAUSAL WOMEN. *Yan Song, Nai-Chieh You, Yiqing Song, Mo Kang, Lifang Hou, Robert Wallace, Charles Eaton, Lesley Tinker, Simin Liu (University of California, Los Angeles, Los Angeles CA 90095)

Background: Dietary factors, including dietary fat, may affect the biological aging process as reflected by the shortening of telomere length (TL) by affecting levels of oxidative stress and inflammatory responses. Objective: We examined the direct relations of total and types of dietary fats and fat-rich foods to peripheral leukocytes TL in a cross-sectional study. Design: In 4029 apparently healthy postmenopausal women who participated in the Women's Health Initiative, leukocyte TL was measured by quantitative PCR. Intakes of total fat, types of fatty acids, and fat-rich foods were assessed by a food frequency questionnaire. Results: Intake of short-to-medium chain saturated fatty acids (aliphatic tails of ≤12 carbons, SMSFA) were inversely associated with TL: in multivariable adjusted model, women who were in the highest quartile of SMSFA intake (median: 1.29% of energy) had the shortest TL (mean: 4.01 kb; 95% CI: 3.90, 4.11 kb), whereas women in the lowest quartile of intake (median: 0.29% of energy) had the longest TL (mean: 4.15 kb; 95% CI: 4.04, 4.25 kb). Except for lauric acid (12:0), all other individual SMSFA were inversely associated with TL after multivariable adjustment (all P < 0.05). In isoenergetic substitution models, substitution of 1% of energy from SMSFA to any other energy sources was associated with 124 base pairs longer TL (95% CI: 34, 214 bp). Intake of non-skim milk, butter, and whole-milk cheese (major sources of SMSFA) were all inversely associated with TL. No significant associations were found with long chain saturated fatty acids, MUFA, and PUFA. Conclusions: Higher intake SMSFA and SMSFA-rich foods were associated with shorter peripheral leukocyte TL among postmenopausal women.

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INTAKES OF DIETARY FLAVONOIDS AND THYROID CANCER RISK IN A LARGE PROSPECTIVE STUDY. *Qian Xiao, Yikyung Park, Cari Kitahara (National Cancer Institute, North Bethesda MD)

Background: Nutritional factors may affect thyroid cancer development. Experimental evidence suggests that dietary flavonoids influence thyroid carcinogenesis by inhibiting cell proliferation and manipulating the activity of key enzymes in thyroid hormone biosynthesis. To date, only one observational study directly examined the association between dietary flavonoids and thyroid cancer risk and found an inverse association with nutrients enriched in soy-based foods. Method: We examined the risk of thyroid cancer in relation to dietary intakes of catechins, flavanones, flavonols, anthocyanidins, flavones, isoflavones, and total flavonoids in the National Institutes of Health–AARP Diet and Health Study, which includes 491,840 men and women, ages 50 to 71 at baseline in 1995–1996. Dietary intakes were assessed at baseline using a self-administered food frequency questionnaire. Cancer cases were ascertained by linkage to state cancer registries. Multivariable-adjusted Cox proportional hazard models were used to estimate relative risks (RRs) and 95% confidence intervals (CIs). Results: During an average of 9 years of follow up, we identified 586 thyroid cancer cases. Among men, high intake of catechins was associated with significantly decreased risk of thyroid cancer (RR Q5 vs Q1, 0.54, 95% CI, 0.36-0.81, p trend, 0.01), while high intakes of flavanones and flavones were associated with significantly increased risk (RR Q5 vs Q1 (95% CI): 1.62 (1.08-2.43) for flavanones, p trend, 0.01; 1.51 (1.00-2.28) for flavones, p trend, 0.04). Significant interactions with smoking were found for catechins, flavonols, and isoflavones in men, with generally inverse associations observed among former and current smokers and positive associations observed among never smokers. No associations between dietary flavonoids and thyroid cancer were found in women. Conclusion: Certain forms of flavonoids may influence thyroid cancer risk in men. The effects may be modulated by smoking.

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MAJOR DIETARY PATTERNS AND CAROTID INTIMA-MEDIA THICKNESS IN BANGLADESH. *Tyler R McClintock, Yu Chen, Faruque Parvez, Fen Wu, Stephanie Segers, Tariqul Islam, Alauddin Ahmed, Rina Rani Paul, Ishrat Shaheen, Golam Sarwar, Tatjana Rundek, Ryan T Demmer, Moise Desvarieux, Habibul Ahsan (New York University School of Medicine, New York NY 10016)

Carotid intima-media thickness (IMT) is a validated surrogate marker of preclinical atherosclerosis and is predictive of cardiovascular morbidity and mortality. Research is lacking on the relationship between dietary patterns and IMT, especially in low-income countries or low-body mass index (BMI) populations. We conducted a cross-sectional analysis in 1149 participants randomly selected for IMT measurement in the Health Effects of Arsenic Longitudinal Study (HEALS) in Araihazar, Bangladesh, from 2010-2011. Dietary intakes were measured using a validated, 39-item food-frequency questionnaire (FFQ) at baseline recruitment of the HEALS cohort. Principal component analysis of reported food items yielded: (i) a balanced diet, comprised of steamed rice, red meat, fish, fruit and vegetables; (ii) a Western diet more heavily weighted towards eggs, milk, red meat, poultry, bread, and vegetables; and (iii) a gourd and root vegetable diet that relied heavily on a variety of gourds, radishes, pumpkin, sweet potato and spinach. We observed a positive association between both the Western and gourd/root vegetable diets and carotid IMT, with corresponding increases of 8.19 μm (95% confidence interval [CI]: 1.62, 14.76; p = 0.02) and 8.76 μm (95% CI: 2.89, 14.64; p < 0.01) per standard deviation increase in pattern adherence, respectively, after controlling for age, sex, total caloric intake, smoking status, BMI, and consumption of individual food items. The balanced pattern was associated with an IMT decrease of 9.06 μm (95% CI: -16.47, -1.65; p = 0.02) per standard deviation of adherence in the same model. These findings show that both Western and gourd/root vegetable diets in this Bangladeshi population positively correlate with carotid IMT, while a balanced diet is associated with decreased IMT.

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RELATIONSHIP OF SERUM CAROTENOID CONCENTRATIONS WITH ALLOSTATIC LOAD AMONG MIDDLE AGED ADULTS IN THE UNITED STATES: THE THIRD NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES III).

*Natalya Rosenberg, Kamal Eldeirawi (College of Nursing University of Illinois, Chicago, Chicago IL 60612)

Carotenoids have been linked with individual cardiovascular, metabolic, and inflammatory markers of disease. However, little is known about the effect of carotenoids on allostatic load, an indicator of the negative cumulative effect of lifetime environmental stress on the biological stress adaptation capacity. The purpose of this study was to examine the association of serum concentrations of carotenoids with allostatic load among middle-aged (45-64 years, N = 3,347) men and women who participated in the Third National Health and Nutrition Examination Survey (1988-1994). The outcome was sex-specific allostatic load score, based on 9 risk-rated indicators (systolic and diastolic blood pressure, pulse rate, total and high density cholesterol, glycosylated hemoglobin, sex-specific waist-to-hip ratio, albumin and C-reactive protein). Allostatic load was categorized as high when two or more indicators were in the high risk category. In logistic regression analysis, beta-carotene and total carotenoids were inversely associated with high allostatic load, in a dose-dependent manner, after adjusting for education, race-ethnicity, serum cotinine, alcohol consumption, vitamin/mineral supplementation, physical activity, and other carotenoids (alpha-carotene, beta-cryptoxanthin, lycopene, lutein/zeaxanthin). Males in the lowest beta-carotene and total carotenoid quartiles were 2.06 [95% confidence interval, CI 1.29-3.29] and 1.58[95% CI 1.11-2.24] times as likely to have high allostatic load, compared to their male peers in the highest quartile. The respective odds ratios for females were 2.73 [95% CI 1.71-4.35] and 2.11[95% CI 1.53-2.92]. Low total carotenoid status is related to the broad physiologic dysregulation from lifetime stress exposure among middle aged adults. More research is needed to further explore the role of carotenoids in the physiological adaptation to environmental stress.

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INDIVIDUAL AND NEIGHBORHOOD-LEVEL POVERTY, SEGREGATION AND DIET: FINDINGS FROM A POPULATION-BASED SURVEY OF NYC ADULTS.

*Stella Yi, Ryan Ruff (New York City Department of Health & Mental Hygiene, Queens NY 11101)

Consuming less sodium (Na) and more potassium (K) through diets low in processed foods reduces cardiovascular disease risk. Dietary intake may be affected by neighborhood-level poverty, with fast food and other less-healthy options more prevalent in high-poverty areas. Racial segregation has been shown to be associated with both poor, and healthier dietary habits but data are limited. This study presents relationships between individual-level poverty and Na, K, and Na:K ratios, and explores potential interaction with neighborhood-level poverty and segregation using two-level hierarchical linear models. Data from the 2010 Heart Follow-Up Study, a cross-sectional study with 24-hour urine collection data and self-reported health behaviors (n = 1656), were analyzed. Neighborhood-level poverty and segregation were defined by aggregated zip-code areas. Degree of racial segregation was measured with the isolation index, describing minority group member exposure to one another. Scaled weights were included to accommodate clustering and disproportionate sampling. Individual-level poverty was associated with higher Na intake and Na:K ratios after adjustment for neighborhood-level poverty and segregation. Na intake and Na:K ratios were higher in very high vs. low poverty neighborhoods. Hispanics in highly segregated neighborhoods had higher K intake, lower Na intake, and lower Na:K ratios than non-segregated Hispanics. Individual-level poverty significantly interacted with segregation; compared to high-income peers, low-income segregated Asians had lower Na:K ratios, while low-income segregated Hispanics had higher ratios. The impact of individual-level income on Na and K intake may be modified by segregation, particularly in Asian and Hispanic ethnic enclaves. Practical consideration of neighborhood composition may enhance impact of dietary behavior change interventions.

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TRENDS IN MEAT INTAKE OVER 17 YEARS IN RELATION TO DIABETES, WEIGHT GAIN, AND WEIGHT LOSS.

*Pramil Singh, Diamond Nguyen, Joan Sabate (Center for Health Research, Loma Linda CA 92354)

Background. There is a paucity of population-based prospective data relating changes in the vegetarian diet to changes in adiposity. One limitation of studies of vegetarians is the unknown causal effect of the foods substituted for meat. Due to faith-based counsels on health, Seventh-day Adventists in a long running cohort study were found to commonly avoid meat, and eat plant foods such as nuts, legumes, and soy. Our aim was to examine how vegetarianism over a 17 year interval status was associated with diabetes and weight change. Methods. As part of the Adventist Health Study-1 (AHS-1) and Adventist Mortality Study (AMS), data on diet and diabetes occurrence were gathered among 7165 Seventh-day Adventists who completed questionnaires in 1960 and in 1976. We identified 468 new diabetes cases in 1976. Results. An increase in meat intake (zero to weekly intake) was associated with a two-fold increase in odds of diabetes (OR = 2.66; 95% CI = 1.79-3.95) and three-fold increase in odds of gaining 10 kg or more (OR = 3.31 95% CI = 2.26-4.86). Weekly meat intake over a 17 year interval was associated with a two-fold increase in odds of weight gain (OR = 1.98 95% CI = 1.55-2.54). A decrease in meat intake from weekly to no meat intake was associated with a 2-fold increase in odds of weight loss (OR = 2.35 95% CI = 1.55-3.56). Conclusion. Weekly meat intake as s stable diet pattern or as a result of an increase in meat intake was associated with diabetes and weight gain over a 17 year interval. Close study of the plant foods consumed in the meatless diets practiced in the AMS and AHS-1 cohorts could potentially provide further insight into dietary practives for prevention of diabetes and obesity.

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DIETARY N-6 POLYUNSATURATED FAT, CARBOHYDRATE-TO-PROTEIN RATIO, AND CHANGE IN BODY WEIGHT AND WAIST CIRCUMFERENCE: A FOLLOW-UP STUDY.

*M U Jakobsen, L Madsen, C Dethlefsen, K M Due, J Halkjær, T I A Sørensen, K Kristiansen, K Overvad (Department of Public Health, Section for Epidemiology, Aarhus University, Aarhus, Denmark)

The balance between carbohydrate and protein in the diet may determine the effect of intake of n-6 polyunsaturated fatty acids (PUFA) on body fat mass; n-6 PUFA may decrease fat mass at a low carbohydrate-to-protein ratio, but increase fat mass at a high ratio. We investigated the association between the intake of n-6 PUFA and subsequent change in body weight and waist circumference at different levels of the carbohydrate-to-protein ratio. Women and men (n = 29,152) were followed for a median of 5.3 years. We applied linear regression models with a 5-y change in weight or waist circumference as the outcome, including a two-way interaction term between n-6 PUFA and carbohydrate intakes, lower-order terms, protein intake, long-chain n-3 PUFA intake, and other potential confounders. Due to adjustment for intake of protein, levels of carbohydrate may indirectly reflect levels of the carbohydrate-to-protein ratio. For high intake of n-6 PUFA (6.9% energy) versus low intake of n-6 PUFA (3.4% energy), the difference in 5-year weight change was -189.7 g (95% confidence interval (CI): -636.8, 257.4) at a low carbohydrate-to-protein ratio and -86.7 g (95% CI: -502.9, 329.6) at a high carbohydrate-to-protein ratio; the differences in 5-year waist circumference change were 0.26 cm (95% CI: -0.47, 0.98) and -0.52 cm (95% CI: -1.19, 0.15), respectively. Inclusion of the dietary glycemic index did not change the results. In conclusion, no consistent associations between the intake of n-6 PUFA and change in body weight or waist circumference at different levels of the carbohydrate-to-protein ratio were observed.

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LEAN FISH AND SEAFOOD CONSUMPTION DOES NOT PREVENT INCREASES IN BODY WEIGHT, WAIST CIRCUMFERENCE AND PERCENTAGE OF BODY FAT. *Lujing Zhan, Jihong Liu, Duck-chul Lee, Xuemei Sui, Steven Blair (University of South Carolina at Columbia, Columbia SC, 29208)

Fish and seafood are nutrient dense and healthful foods that have been widely recommended. Yet, research on the protective roles of fish and seafood consumption on body weight is still limited and inconclusive. We investigated the association between lean fish and seafood consumption and subsequent change in body weight, waist circumference (WC) and percentage of body fat (%BF) using the data from the Aerobics Center Longitudinal Study. The sample included 3982 participants with baseline data and one additional clinical examination between 1987 and 1999. Fish and seafood consumption was assessed by a 3-day diet record. Body weight, WC, and %BF were measured at clinical exams. We used logistic regression models to investigate the relationships between lean fish and seafood consumption and significant changes in body weight (≥5 pounds), WC (≥3 cm) and %BF (≥3.2) after controlling for sex, age, body mass index, hypertension, hypercholesterolemia, cardiorespiratory fitness, physical activity, smoking, and drinking behaviors at enrollment. We also used linear regression models to examine the associations using continuous measures of weight, WC, and %BF. We found that the mean consumption of lean fish and seafood at enrollment was 35.5 grams/day (±42.3). Approximately 30% participants had significant increases in weight, WC, or %BF over an average of 6.2 years of follow-up (± 4.3). Lean fish and seafood consumption was not associated with significant changes of weight, WC or %BF during the follow-up. When stratified by sex, a weak protective effect of lean fish and seafood consumption on significant weight change was found among women. These results suggest that lean fish and seafood consumption do not prevent increases in body weight and body composition. Recommendations regarding fish and seafood consumption should be considered with other dietary factors, such as dietary patterns, species of fish or seafood, and other foods.

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RACIAL DIFFERENCES IN PLASMA LEVELS OF TOTAL AND FREE 25-HYDROXYVITAMIN D AND VITAMIN D BINDING PROTEIN. *Tianyi Huang, Elizabeth Poole, Eric Taylor, Shelley Tworoger (Department of Epidemiology, Harvard School of Public Health, Boston MA 02115)

Disparities exist for chronic disease incidence between racial groups in the U.S. Total 25-hydroxyvitamin D [25(OH)D] levels, which have been associated with reduced risk of some cancers, diabetes, and heart disease, are known to be lower in African-Americans and Asians versus Caucasians. However, less is known about the differences for vitamin D binding protein (VDBP) and free 25 (OH)D, which may be more biologically relevant. Therefore we examined vitamin D related biomarkers among 111 Caucasians, 111 African-Americans, and 111 Asians matched on age, timing in luteal phase, and date, time, and fasting status at blood collection in Nurses' Health Study II. We used a multivariate mixed model accounting for matching factors and other determinants of plasma vitamin D to analyze the association of race with total and free 25(OH)D, VDBP and molar ratio of 25(OH)D:VDBP. Least squares means of 4 outcomes were compared. Interactions with body mass index (BMI) also were evaluated. Both total 25(OH)D and VDBP levels were highest in Caucasians, lower in Asians and lowest in African Americans ($p < 0.01$ for all pairwise comparisons). Conversely, African Americans and Asians had modestly higher molar ratio and free 25(OH)D levels compared with Caucasians (e.g., free 25(OH)D levels were 21.4, 22.6, and 18.8 pmol/L, respectively). The associations between BMI and vitamin D biomarkers were suggestively different across racial groups (p-interaction < 0.09). BMI was inversely associated with total and free 25(OH)D and molar ratio in Caucasians, positively associated in Asians and not associated in African Americans. This exploratory study suggests that well-established racial differences in total 25(OH)D are not observed for free 25(OH)D, a potentially more biologically active form. Future studies should further confirm our findings and explore the functional differences between total and free 25(OH)D as well as the mechanisms for the race-specific associations with BMI.

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INDEX-BASED DIETARY PATTERNS AND RISK OF HEAD AND NECK CANCER IN THE NIH-AARP DIET AND HEALTH STUDY. *Wen-Qing Li, Yikyung Park, Jennifer Wu, Alisa Goldstein, Philip Taylor, Albert Hollenbeck, Neal Freedman, Christian Abnet (Department of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Rockville MD 20852)

Dietary factors have been associated with cancers of head and neck, but other than alcohol, few associations are convincing. Due to the complexity of the diet, studies of dietary patterns may provide more insight than studies of individual foods. We prospectively evaluated the association of two index-based dietary patterns, the Healthy Eating Index-2005 (HEI-2005) and the alternate Mediterranean Diet Score (aMED), with the risk of head and neck squamous cell carcinoma in 494,967 participants of the US National Institutes of Health-AARP Diet and Health study. We estimated scores for HEI-2005 and aMED based on dietary information collected from a self-reported baseline food frequency questionnaire. Higher scores in each index are thought to reflect healthier eating patterns. During a follow-up of 11 years (1995-2006), 1868 participants were diagnosed with head and neck cancer. After adjusting for smoking, alcohol intake, education, and other potential confounders, we observed a significant decrease in risk of head and neck cancer with the increasing scores of the HEI-2005 in men (hazard ratio (HR): 0.74, 95% confidence interval (CI): 0.61-0.89 for the highest quintile compared to lowest; P-trend across categories = 0.0008) and women (HR: 0.48; 95% CI: 0.33-0.70; P-trend < 0.0001). High scores in aMED were also associated with a reduced risk of head and neck cancer in men (P-trend = 0.002) and women (P-trend < 0.0001). Associations were similar among head and neck cancer subsites, including larynx, oral cavity and oro-hypopharynx. We did not find significant differences in the associations between each index and risk of head and neck cancer across the categories of smoking and alcohol intake. Our results suggest that adhering to dietary recommendations may help prevent head and neck cancer.

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FOOD CONSUMPTION PATTERNS OF VEGETARIANS AND NON VEGETARIANS IN ADVENTIST HEALTH STUDY 2. *Michael Orlich, Joan Sabate, Karen Jaceldo-Siegl, Jing Fan, Pramil Singh, Gary Fraser (Loma Linda University, Loma Linda CA 92350)

Background: Vegetarian diet patterns have been defined by an absence of certain animal foods, but the consumption of other foods may also differ in important ways. We sought to identify how the consumption of various food groups differed among vegetarian-spectrum dietary patterns in Adventist Health Study 2 (AHS-2). Methods: AHS-2 is a cohort of 96,469 Seventh-day Adventists recruited between 2002-2007. Diet was assessed by a quantitative food frequency questionnaire. Diets were classified into five patterns: vegan, lacto-ovo vegetarian, pesco vegetarian, semi vegetarian, and non vegetarian. Individual foods were classified into 45 minor, non-overlapping food groups, which were further clustered into 15 major food groups and 5 broad categories. Mean values, adjusted for age, sex, and race by direct standardization and standardized to 2000 kcal/day by simple division, were compared for the vegetarian diet patterns compared to the non vegetarian diet. Results: Vegetarians consumed less meats, dairy products, and eggs than did non vegetarians, by definition. Additionally, vegetarians consumed substantially less caloric beverages, sweets, and added fats than did non vegetarians; they consumed notably greater amounts of nuts and seeds, soy foods and meat analogues, legumes, grains, potatoes, avocados, vegetables, and fruits. Conclusion: The food consumption patterns of vegetarians differ markedly from those of non vegetarians, beyond their reduced consumption of animal foods, in ways which might have health effects.

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MULTIVITAMIN USE AND CARDIOVASCULAR DISEASE IN A PROSPECTIVE STUDY OF WOMEN. *Susanne Rautiainen, I-Min Lee, J Michael Gaziano, Julie E Buring, Howard D Sesso (Brigham and Women's Hospital and Harvard Medical School, Boston MA 02215)

Although multivitamins are widely used, there are limited prospective studies investigating their association with the long-term risk of cardiovascular disease (CVD). We studied 35,927 women aged 45y or older from the Women's Health Study free of CVD and cancer at baseline. Women self-reported a range of lifestyle and clinical factors and the intake of food and dietary supplements. Women were categorized at baseline as taking: (1) no supplements (2) multivitamins only (3) multivitamins with other vitamin/mineral supplements, and (4) other supplements only. We also considered the duration of multivitamin use. We used Cox proportional hazards models to calculate multivariable-adjusted rate ratios (RR) (95% confidence intervals (CI)). At baseline, 32% were taking multivitamins. Women taking multivitamins only versus no supplements were less likely to currently smoke and more likely to be postmenopausal and physically active. During an average of 15.8y of follow-up, there were 1423 cases of CVD (defined as myocardial infarction (MI), stroke, and CVD death). In multivariable analyses, there were no statistically significant RRs (95% CIs) comparing taking multivitamins only versus no supplements and CVD (1.05 (0.88-1.25)), MI (1.09 (0.82-1.44)), stroke (1.09 (0.85-1.41)), cardiac revascularization (1.07 (0.89-1.29)) or CVD death (1.10 (0.77-1.59)). Similar associations were observed for women using multivitamins with other supplements. Multivitamin use >10y was also not significantly associated with CVD. There was no effect modification of multivitamin use only and CVD by age, body mass index and smoking status. Among women consuming <4 servings/day of fruits and vegetables, multivitamin use only had a potential inverse association with total CVD (RR (95% CI) = 0.48 (0.24-0.97)) but the interaction was not significant. In conclusion, multivitamin use does not appear to be associated with risk of developing CVD in middle-aged and older women.

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ASSOCIATION BETWEEN BREASTFEEDING AND INFANT GROWTH: A PROBABLE REVERSE CAUSALITY. *Shraddha Vyas, Jihong Liu, Wilfried Karmaus, Hongmei Zhang, Nelis Soto-Ramirez (University of South Carolina, Arnold School of Public Health, Columbia SC 29208)

The association between breastfeeding and infant growth show debatable results with regards to temporal sequence. The study aimed at examining the association between breastfeeding and infant growth and investigating the possible reverse causality in this association. Data came from the Infant Feeding Practices Survey II, a national longitudinal database among women recruited prenatally and followed until one year of infants life from May 2005 through June 2007 (N = 2914). Mixed linear model was used to assess the impact of breastfeeding from the 2nd, 4th, 6th and 9th months on infant growth (weight-for-age z- score (WAZ), length-for-age z-score (LAZ), and weight-for-length z-score (WLZ)) from the 3rd, 5th, 7th and 12th months. Reverse causation was evaluated with a log-linear model using infant growth data from the 3rd, 5th and 7th months and breastfeeding data from 4th, 6th and 9th months, restricting to infants breastfed in the 3rd, 5th and 7th months or those who were exclusively breastfed in the first 5 months. Mean WAZ of non-exclusively breastfed infants increased steeply from 3rd month (0.10) to 7th month (0.34), while WAZ among exclusively breastfed infants WAZ was stable (0.27 to 0.24) (p for interaction = 0.003). Non-breastfed infants had a higher WAZ throughout the first year (3rd month = 0.20, 12th month = 0.67) than infants who were ever breastfed in the first year (3rd month = 0.04, 12th month = 0.29) (p for interaction <.0001). Similar results were seen for WLZ (p for interaction = 0.006). Log-linear model showed that one unit increase in WAZ was associated with a 7% (95% Confidence Interval 1.00, 1.14) higher risk of continuing with exclusive breastfeeding. Our findings show that exclusively breastfed infants have a better WAZ in the earlier months. Some evidence of reversal causality was seen with WAZ and exclusive breastfeeding, but not LAZ and WLZ measures, suggesting weight gain to bea predictor of continuation of exclusive breastfeeding.

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TRIGGERS OF SPONTANEOUS PRETERM DELIVERY: WHY DID IT HAPPEN TODAY? *Caroline E Boeke, Brian T Bateman, Anna Thornton, Brett Young, Andrea V Margulis, Thomas F McElrath, Jeffrey L Ecker, Sonia Hernandez-Diaz (Harvard School of Public Health and Channing Division of Network Medicine, Brigham and Women's Hospital, Boston MA 02115)

Little is known about immediate causes of spontaneous preterm delivery. We sought to identify triggers using a case-crossover design. We enrolled 50 women with preterm labor (PTL) and 50 with preterm premature rupture of membranes (PPROM) admitted to the Massachusetts General Hospital between September 2011 and June 2012. We enrolled a control group of 158 pregnant women at their regular prenatal care visits matched to cases by gestational age and calendar time. The index time was defined as onset of PTL/PPROM (for case subjects) or interview (for control subjects). Detailed information was collected through structured interviews about factors of interest in the 72 hours preceding the index time. We compared the frequency of transient factors from case (0-24 hours before index time) and control (48-72 hours before) windows within case subjects. Both chronic and transient characteristics were compared between case and control subjects. Matched odds ratios (ORs) and 95% confidence intervals (CIs) were estimated with conditional logistic regression. PTL/PPROM onset appeared to be related to circadian patterns. We confirmed previously hypothesized associations of chronic risk factors with spontaneous preterm delivery, including mood disorders and stressful events, which were more common in cases than controls. Within cases, skipped meals (OR 4.3; 95% CI 1.2-15.2), disturbed sleep (4.5; 1.5-13.3), sexual activity (6.0; 0.7-69.8) and spicy food (7.0; 1.6-30.8) were associated with increased risk in the following 24 hours. For other triggers evaluated, including physical exertion, the OR was close to the null. Due to few discordant pairs, confidence intervals were wide. Lost appetite and disturbed sleep may predict imminent preterm delivery; sexual activity may trigger preterm delivery in susceptible women. Larger case-crossover studies may adequately assess the impact of modifiable triggers on spontaneous preterm delivery and help guide obstetrical care.

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ADJUSTING FOR A COLLIDER CAN BE A SIN WORTH COMMITTING: AN EXAMPLE FROM REPRODUCTIVE PERINATAL EPIDEMIOLOGY. *Olga Basso, Allen Wilcox, Clarice Weinberg (McGill University, Montreal QC Canada)

When estimating the direct effect of an exposure on neonatal death, adjustment for length of gestation can cause serious bias. This is because rare but strong unmeasured factors influence gestational length and account for a large fraction of mortality. Investigators also routinely adjust for gestational length when analyzing birth weight, to remove the strong effect of early delivery on weight at birth. But does such adjustment introduce collider bias? We explored this question in a simulation, creating a population of babies in which each baby has a target birth weight (3500 g ± 450g at 40 weeks) and a target gestational length (40 weeks or 280 days, ± 10d), all based on normal distributions. A measured exposure (E) decreases target birth weight by 270g (±30g) and gestational length by 20 days (±7d). Two "unmeasured" factors (U1 and U2), each occurring in 4% of babies, decrease target gestational length (by 50 and 35 days, respectively) and target birth weight (by 1000g and 600g). We applied Gardosi's proportionality formula (1995) to derive, for each simulated baby, the birth weight achieved at the attained gestational length after including the effects of the above factors. We then estimated the effect of E through linear regression, comparing a "full" model (including a cubic function of gestational age and all the factors, with their cross-products with gestational age) with a model ignoring U1 and U2. Compared with the (unbiased) estimate of E obtained in the full model, the collider-adjusted estimate omitting U1 and U2 resulted in modest bias (10% or less). When continuous birth weight is the outcome, adjustment for gestational length does not appear to cause substantial bias even when unmeasured factors have a strong effect on both duration of gestation and birth weight.

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APPETITE, DIETARY INTAKE, AND GESTATIONAL WEIGHT GAIN.

*Fu-Ying Tian, Xiao-Zhong Wen, Cai-Xia Zhang, Chuan-Bo Xie, Jianmiao Lin, Shi-Xin Yuan, Li-Hua Chen, Bao-Zhen Huang, Xiao-Ling Guo, De-Qin Jia, Wei-Qing Chen (Department of Biostatistics and Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou Guangdong China)

Objective: To investigate the effect of appetite after 20 gestational weeks and diet on the gestational weight gain (GWG). Methods: We analyzed the data of 3,525 women in the Guangdong Pregnant Women Health Survey conducted during 2009-2010 in Southern China. The pregnant women retrospectively self-reported their appetite (bad, average, and good) after 20 weeks of gestation, and food, beverage, dietary supplement intake during pregnancy. GWG was defined as the difference between self-reported pre-pregnancy weight and measured pre-delivery weight. We fitted multivariable linear regression model for the associations of appetite and dietary intake with GWG, adjusting for family income, maternal age, education, occupation, marital status, pre-pregnancy body mass index, physical activity during pregnancy, and the gender of child and gestational age. Results: In univariate analyses, higher intake of egg, bean, milk, fish, vegetable was associated with higher GWG (P-value < 0.05). Maternal better appetite after 20 weeks of gestation (good vs. bad, 1.62 kg [95% confidence interval, 0.90 to 2.34]), calcium supplement use (ever vs. never, 0.67 kg [0.27 to 1.08]), egg intake (2-4 per day vs. <2 per day, 0.79 kg [0.35 to 1.24]), beans intake (100g-200g per day vs. never, 0.70 kg [0.09 to 1.31]) was associated with higher GWG. In contrast, maternal tea drinking during pregnancy (ever vs. never, -0.67 kg [-1.15 to -0.18]) was associated with lower GWG. Conclusion: Better appetite, calcium supplement, and egg intake might increase GWG, whereas tea drinking might restrict GWG. Our findings can inform dietary intervention to achieve healthy GWG.

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MENSTRUAL CYCLE CHARACTERISTICS IN RELATION TO PLASMA STEROID HORMONE, PROLACTIN, AND GROWTH FACTOR CONCENTRATIONS IN PREMENOPAUSAL WOMEN.

*Fan Mu, A Heather Eliassen, Shelley S Tworoger, Susan E Hankinson, Stacey A Missmer (Harvard School of Public Health, Boston MA 02115)

Background: Menstrual cycle characteristics are risk factors for reproductive pathologies, perhaps through the hormonal milieu. Studies on menarche and hormones have conflicted, and other characteristics are minimally explored. Methods:We assessed whether age at menarche, cycle length and regularity at age 18-22 were associated with plasma estrogens, androgens, progesterone, prolactin, sex hormone binding globulin(SHBG), growth hormone, insulin-like growth factor-I, and its binding protein-3, in 2708 premenopausal women in the Nurses' Health Study 2, aged 32-52 at blood draw. Estrogens and progesterone were from timed samples;all others in timed or untimed samples. General linear models yielded geometric means. Models adjusted for assay batch;age, fasting, time of day, month, ovulatory status, and luteal day at draw;and past oral contraceptive use. Results: Age at menarche was inversely associated with free testosterone(>13 vs <12 years = 14%, Ptrend = 0.002), and directly associated with SHBG(17%, Ptrend < 0.0001). Trends were attenuated with body mass index adjustment. Cycle length at age 18-22 was inversely related to follicular total estradiol (%difference >39 vs <26 days = 16%, Ptrend = 0.01), and directly with free testosterone(17%, Ptrend = 0.02). Cycle regularity at age 18-22 was associated with follicular free estradiol(irregular vs very regular = 13%, Ptrend = 0.005) and follicular estrone(7%, Ptrend = 0.03). These associations remained unchanged after exclusion of anovulatory, irregular cycles and cycles with extreme luteal days or additionally adjusting for body size. No associations were observed with other hormones. Conclusion: These data suggest that early adulthood menstrual characteristics are associated with hormone concentrations during the mid-late reproductive years, but with modest magnitudes, playing a minor role in the relationships between menstrual characteristics and reproductive pathologies.

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THE ASSOCIATION BETWEEN LATE PRETERM AND EARLY TERM BIRTH AND NEONATAL INTENSIVE CARE UNIT TRIAGE/ ADMISSION: THE ROLE OF THE BIOLOGICAL DETERMINANTS OF EARLY DELIVERY.

*Hilary K Brown, Kathy Speechley, Jennifer Macnab, Renato Natale, M Karen Campbell (Department of Epidemiology and Biostatistics, The University of Western Ontario, London ON Canada)

It is unclear to what extent poor outcomes among infants born late preterm (34-36 weeks) and early term (37-38 weeks) are associated with physiological immaturity or with conditions that led to early delivery. The objective of this analysis was to determine whether the biological determinants of preterm birth, such as infection and placental ischemia, modify the effect of gestational age on the risk of neonatal intensive care unit triage/admission. Data from the London Health Sciences Centre (London, Canada) perinatal database were linked with data from the discharge abstracts database. The sample included singleton live births, delivered at 34-41 weeks and with no major congenital anomalies (N = 38,807). Multivariable models were built using modified Poisson regression. Additive interactions between gestational age (late preterm, early term vs. full term) and the biological determinants of preterm birth were assessed by calculating the relative excess risk due to interaction (RERI). The joint effect of gestational age and placental ischemia on neonatal intensive care unit triage/admission was greater than additive for late preterm birth (adjusted RERI = 2.35, 95% CI 1.22, 3.55) and for early term birth (adjusted RERI = 0.85, 95% CI 0.49, 1.22). Similarly, the joint effect of gestational age and other determinants (diabetes, premature rupture of the membranes) was greater than additive for late preterm birth (adjusted RERI = 1.73, 95% CI 0.49, 3.12) and for early term birth (adjusted RERI = 0.75, 95% CI 0.28, 1.24). The joint effect of gestational age and infection was less than additive. These findings demonstrate that among 'near term' deliveries, there are high risk groups, defined by the conditions leading to early delivery, which are at even greater risk for poor outcomes.

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BREASTFEEDING AND LONG-TERM MATERNAL WEIGHT GAIN IN A PROSPECTIVE COHORT OF AFRICAN AMERICAN WOMEN.

*Julie Palmer, Kristen Kipping-Ruane, Lauren Wise, Lynn Rosenberg (Slone Epidemiology Center at Boston University, Boston MA 02215)

It has been hypothesized that breastfeeding may reset maternal metabolism, resulting in increased mobilization of stored fat after delivery and long-term altered glucose homeostasis. We examined whether African American women who breastfed their first baby gained less weight 4 and 8 years after giving birth than did women who had not breastfed. In the Black Women's Health Study, a prospective cohort study begun in 1995, 2,940 women had their first child during follow-up and were followed for at least 4 subsequent years. They provided data on weight (every 2 years), height, gestational weight gain (GWG) in the index pregnancy, breast feeding (no, yes, number of months), usual diet, education, and physical activity. Differences in weight gain for women who breastfed 1-2, 3-5, 6-11, or ≥12 months relative to women who did not breastfeed were computed, with control for potential confounders. Overall, 4-year and 8-year mean weight gains were 5.9 kg and 7.9 kg, respectively. 4-year weight gain decreased with increasing months of lactation (p trend < 0.01); the mean difference in weight gain between women who breastfed ≥12 months and those who did not breast feed at all was -2.39 kg (95% CI -3.35, -1.45). Mean differences for ≥12 months lactation relative to none were highest among the subgroups of women who were under age 30 (-2.48 kg, 95% CI -4.74, -0.23), who were not obese before becoming pregnant (-1.97 kg, 95% CI -2.97, -0.96), and who had a GWG of ≥15.9 kg, greater than the highest weight gain recommended by the Institute of Medicine (-3.13 kg, 95% CI -5.19, -1.07). Similar patterns were observed for 8-year weight gain, although estimates were less precise. These findings indicate that African American women who breastfeed their first child have a reduced weight gain during a critical period when women often gain or retain excess weight.

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INFERTILITY TREATMENT AND POSTPARTUM DEPRESSIVE SYMPTOMS IN MASSACHUSETTS. *Sarah Stone, Hafsatou Diop, Eugene Declercq, Howard Cabral, Lauren Wise (Boston University School of Public Health, Westwood MA 02090)

Background: The impact of successful infertility treatment (IFT) on the prevalence of postpartum depressive symptoms (PDS) is uncertain. Methods: We used the Massachusetts Pregnancy Risk Assessment Monitoring System (PRAMS) 2007-2010 data to evaluate whether IFT was associated with early PDS and subsequent help-seeking behaviors. We categorized IFTs into 3 groups: fertility-enhancing drugs (FD), donor insemination or intrauterine insemination (DI/IUI), and assisted reproductive technology (ART) including in vitro fertilization. We defined PDS as report of 'always' or 'often' to any depressive symptoms; reference group reported 'sometimes', 'rarely' or 'never' to all depressive symptoms. Modified Poisson regression models directly estimated prevalence ratios (PRs) and 95% confidence intervals (CIs), controlling for socioeconomic status indicators and prior mental health visits. Results: Among 3,509 participants in PRAMS during 2007-2010 who wanted pregnancy, 11.7% reported any IFT (FD = 6.0%, DI/ IUI = 2.6%, ART = 4.9%, weighted using SUDAAN). Reported IFT was not associated with an appreciable increase in prevalence of PDS (PR = 1.13, 95% CI 0.78-1.63). Grouped IFTs also showed no material increase in prevalence of PDS: FD PR = 1.14 (95% CI 0.58-2.24), DI/ IUI PR= 1.16 (95% CI 0.47-2.85), ART PR = 0.82 (95% CI 0.41-1.62. Among those with PDS, there was little evidence that any type of IFT predicted help-seeking behavior. Conclusions: IFT was not associated with increased prevalence of early PDS. Moreover, IFT did not predict help-seeking behavior among women with PDS. While reassuring women that IFT does not increase prevalence of PDS, all mothers should be continuously screened postpartum and encouraged to seek help for effective primary prevention of PDS.

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SPATIAL ANALYSIS OF GASTROSCHISIS IN TEXAS AND MASSACHUSETTS. *Mahsa M Yazdy, Veronica M Vieira, Peter H Langlois, Marlene Anderka, Martha M Werler (Slone Epidemiology Center at Boston University, Boston MA 02215)

Gastroschisis is a congenital malformation where loops of bowel are protruding from the abdominal wall. Previous research has suggested that gastroschisis cases can occur in clusters. The objective of this study was to identify clusters of gastroschisis in space or the combination of space and time. Cases of gastroschisis were identified from the birth defect registries in Massachusetts and Texas. In each state, a random sample of live-births was selected as controls. Generalized additive models (GAMs) were used to create a continuous map surface of odds ratios (OR) by smoothing over latitude and longitude. Using data from birth certificates, insurance status (MA only), maternal age, race/ethnicity, years of education, and cigarette smoking were assessed for adjustment. Permutation tests were used to assess the significance of location and identify locations with statistically significant increased or decreased ORs. In Massachusetts a statistically significant area of increased risk (OR = 2.4) was identified in the north-central part of the state. After adjustment for maternal age and race/ethnicity, the OR decreased to 1.3 and was no longer statistically significant (p-value: 0.07). In Texas, two statistically significant areas of increased risk (ORs = 1.6) were identified and remained significant (p-value <0.001) after adjustment for maternal age and race/ethnicity, though they were attenuated to 1.3 in these areas. Texas had sufficient data to assess the combination of space and time, which identified an increased risk (OR = 2.9) in the center of Texas in 2003. Exploration of possible artifactual, environmental, or behavioral factors in these areas may further our understanding of the etiology of gastroschisis.

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DEMOGRAPHIC, BEHAVIORAL, AND REPRODUCTIVE HISTORY DIFFERENCES BY MATERNAL WORKING STATUS BEFORE AND DURING PREGNANCY: IMPLICATIONS FOR REPRODUCTIVE STUDIES. *CM Rocheleau, SJ Bertke, CC Lawson, PA Romitti, TA Desrosiers, AJ Agopian, EM Bell, SM Gilboa (National Institute for Occupational Safety and Health, Cincinnati OH 45213)

Studies of occupational exposures among reproductive-aged women must address biases that could be caused by self-selection to employment. Data from controls in the National Birth Defects Prevention Study with births from 1997-2007 were used, representing a random sample of live births unaffected by birth defects. We compared personal and household characteristics of women who held any job during the 3 months prior to conception through the end of pregnancy (n = 5978, 71.7%) to those of women who did not hold any job in this period (n = 2365, 28.3%). Patterns of maternal work were also evaluated, including: frequency of part-time, full-time, and long work hours; job change; and job cessation. Most women who did not work during this period self-identified as homemakers/parents (80.4%) or students (14.1%); few reported being disabled (1.2%) or between jobs/unemployed (3.5%). Maternal age, parental race, parental nativity, parental education, and household income differed between families of working and nonworking women. Non-working women were more likely to be multiparous compared to working women (73.8% vs. 54.4%). Working women were more likely to have planned their index pregnancy and have used fertility drugs or treatments to conceive, however they were also more likely to report pregnancy risk behaviors including not using a folic acid supplement during the periconceptional period, smoking, drinking alcohol, and paternal (but not maternal) use of illicit drugs. These patterns could introduce bias in studies of occupational exposures in relation to reproductive outcomes that are not restricted to workers only.

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THE ROLE OF PRE-PREGNANCY BODY MASS INDEX AND GESTATIONAL WEIGHT GAIN IN PRENATAL AND POSTPARTUM DEPRESSION. *Karen Ertel, Tamarra James-Todd, Sheryl Rifas-Shiman, Ken Kleinman, Emily Oken, Janet Rich-Edwards, Matthew Gillman (University of Massachusetts Amherst, Amherst MA 01003)

In non-pregnant populations, overweight and obesity predict development of depression. This association has been less studied in the perinatal period; however, given the dramatic changes in weight experienced in the perinatal period and the high prevalence and important sequelae of perinatal depression, understanding these relationships is critical for promoting maternal and child health. Our objective was to examine the associations of pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) with prenatal and postpartum depression. Study subjects were 1114 Boston-Area women in Project Viva, a prospective cohort study. We calculated P.BMI from self-reported weight and height and used NHLBI definitions to categorize underweight, normal, overweight, obese. GWG was the difference between weight at delivery and pre-pregnancy weight, classified according to 2009 Institute of Medicine recommendations. We assessed depression at mid-pregnancy and 6 months postpartum with the Edinburgh depression scale; score >12 indicated depression. The majority (63%) had normal BMI, 21.9% were overweight, and 11.9% were obese. Ninety (8.1%) women experienced prenatal depression and 57 (5.1%) experienced postpartum depression without prenatal depression. In multivariable logistic regression models adjusted for sociodemographic and health factors, being overweight (v. normal weight) before pregnancy was associated with elevated odds of prenatal depression (OR = 1.9; 95% confidence interval (CI):1.2-3.3) but not postpartum (OR = 0.8; 95% CI: 0.4, 1.8). Obese BMI was associated with postpartum depression (OR= 2.3; 95% CI: 1.1-4.6) but not prenatal OR = 1.1; 95% CI 0.5, 2.3). We did not detect an association of GWG with prenatal or postpartum depression or an interaction between BMI and GWG. Being overweight or obese before pregnancy may increase risk of perinatal depression, suggesting the importance of pre-pregnancy and inter-partum efforts to achieve a healthy weight.

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RELIABILITY OF MOTHER'S REPORTS OF AGE AT WEANING: EVIDENCE OF RECALL BIAS USING DATA FROM THE OREGON PREGNANCY RISK ASSESSMENT MONITORING SYSTEM (PRAMS) AND PRAMS-2. *Marit Bovbjerg, Adrienne Uphoff (Oregon State University, Corvallis OR 97333)

It is well established that breastfeeding benefits both mother and child. Most such beneficial outcomes—e.g., reduced otitis media, reduced risk of breast cancer—are reported to have a dose-response relationship, with a longer duration of breastfeeding being associated with more benefit. Such studies usually rely on retrospective reporting of breastfeeding duration by the mother, though test-retest reliability of these reports has not been studied extensively, particularly when the interval between reports is longer than a few months. Oregon re-contacts PRAMS participants when the children are 2 years old (PRAMS-2). Breastfeeding questions are asked on both surveys. We took the initial PRAMS responses, gleaned when children were around 14 weeks old, to be the gold standard, and compared PRAMS-2 responses. The positive predictive value for "ever breastfed" was 97.6%, but the negative predictive value was only 33.6%. Among mothers who weaned by 14 weeks, only 53.1% (95% confidence limits: 47.9%, 58.4%) reported on PRAMS-2 a duration of breastfeeding that fell within 1 month of their original PRAMS answer. Reliability was higher among mothers with at least some college [57.2% (50.2, 64.2) vs. 51.9% (44.1, 59.8)] and married women [60.0% (53.2, 66.8) vs. 45.3% (37.4, 53.3)]; there was no difference by immigration status. In nearly all instances (95.1%; 92.3, 97.4), the direction of the discrepancy was for mothers to report a longer duration of breastfeeding on PRAMS-2. We conclude that retrospective 'ever breastfed' questions might underestimate the true proportion of ever breastfed infants, and that single-item retrospective questions about breastfeeding duration appear to be strongly biased in favor of reporting more breastfeeding in this population. Our results indicate more bias than has been reported by others. Though not surprising, this has implications for breastfeeding research practice and interpretation.

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EARLY PREGNANCY MATERNAL DIETARY FISH INTAKE AND PREGNANCY COMPLICATIONS: THE OMEGA STUDY. *April Wicks, Mary Lou Thompson, Tom Burbacher, David Siscovick, Michelle Williams, Daniel Enquobahrie (University of Washington-Epidemiology, Seattle WA 98195)

Background: Results from investigations of dietary fish (and subtypes) and pregnancy complications are inconsistent. We investigated associations of early pregnancy dietary fish intake with pregnancy complications. Methods: Among participants (N = 3355) of the Omega study, a prospective cohort study of dietary risk factors for pregnancy complications, in Seattle, Washington (1996-2008), a food frequency questionnaire was used to assess early pregnancy intake of dietary fish and subtypes (fried, shell, white, and dark fish). Information on pregnancy complications, including preeclampsia (PE), gestational hypertension (PIH), gestational diabetes (GDM), and preterm birth (PTB) was obtained from medical records. We used generalized linear models with a log-link, the Poisson family and robust standard errors, to estimate relative risks (RRs) and 95% confidence intervals (CI). Results: Amount or frequency of total fish consumption was not associated with pregnancy complications. Higher intake of fried fish was associated with a higher, though statistically insignificant, risk of pregnancy complications (PE and PIH). Higher intake of shellfish was associated with lower risk of PTB. Women who reported intake of ≥3 servings/week had a 39% lower risk of PTB compared with women who reported intake of <1 servings/week (95% CI:0.39-0.98). White fish consumption was associated with higher risk of GDM (RR:2.81; 95% CI:1.81-6.70 comparing the highest with the lowest intake), but not the other pregnancy complications. Consumption of dark fish was negatively associated with risk of GDM. The adjusted RRs comparing ≥3 servings/week to <1 serving/month of dark fish was 0.38 (95% CI:0.19-0.78) for GDM. Conclusion: The risk of pregnancy complications varies by the type of fish consumed in early pregnancy.

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RISK OF NEONATAL MORBIDITY AMONG INFANTS BORN TO REFUGEE AND NON-REFUGEE IMMIGRANT WOMEN IN ONTARIO, CANADA. *Susitha Wanigaratne, Marcelo Urquia, Donald C Cole (Centre for Research on Inner City Health, St.Michael's Hospital, Toronto ON Canada)

Background: Little is known about adverse maternal and infant health outcomes among refugees immigrating to various countries around the world, including Canada. Objectives: To determine whether infants born to refugee women are at increased risk of neonatal morbidity compared to infants born to non-refugee immigrant women arriving in the province of Ontario, Canada. Methodology: We linked two population-based databases (1988-2010), the Ontario portions of the: Discharge Abstract Database containing diagnostic information on all hospital delivery-birth admissions; and the Citizenship & Immigration Canada database, which contains objective information on most legal immigrants, their refugee status and socio-demographic characteristics. Multiple logistic regression analysis was used to examine risk of eight neonatal morbidity outcomes across the whole time period and for four categories of maternal length of residence. Odds ratios (OR) were adjusted for maternal characteristics such as age, income, education and knowledge of official languages at immigration, year of immigration and year of birth. Results: Risk of three out of eight neonatal morbidities were significantly higher among infants born to refugee women (n = 72,776) compared to non-refugee immigrant women (n = 443,755). The higher risks were found for the following outcomes: respiratory conditions (OR = 1.09, 95% CI 1.06-1.12) which remained significant after adjustment; congenital anomalies (OR = 1.05, 95% CI 1.02-1.09); and hospital readmission due to inadequate weight gain (OR = 1.16, 95% CI 1.03-1.32). The risk of respiratory conditions was significantly higher among infants born to refugee women who gave birth within ten years of migration to Canada. Conclusion: In Canada, refugees are at slightly higher risk of neonatal morbidity compared to non-refugee immigrants. These findings may assist health care practitioners in identifying specific neonatal morbidities of concern in refugee populations.

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HEALTH BEHAVIORS OF INACTIVE PREGNANT WOMEN AT HIGH RISK FOR GESTATIONAL DIABETES MELLITUS. *Carrie Nobles, Bess Marcus, Edward Stanek, Glenn Markenson, Lisa Chasan-Taber (University of Massachusetts Amherst, Amherst MA 01003)

Despite evidence associating moderate exercise during pregnancy with reduced risk of gestational diabetes mellitus (GDM), few studies have investigated the health behaviors and beliefs of inactive pregnant women at high risk for GDM. We evaluated these factors among participants in the Behaviors Affecting Baby and You (B.A.B.Y.) Study (n = 309, 2007-2012), a randomized controlled trial conducted among prenatal care patients at high risk for GDM (i.e., personal history of GDM; or body mass index (BMI) ≥25 kg/m^2 and family history of type 2 diabetes mellitus) and not participating in ≥30 minutes/day of moderate-intensity activity on most days of the week. Data on demographics, lifestyle factors and health beliefs were collected through self-report at enrollment (mean = 12.2 ± 3.3 weeks gestation). The majority of women were young (46.3% < age 25), Hispanic (55.0%), unmarried (65.4%) with low income (37.2% ≤$15,000/year) and education (24.9% did not graduate high school). A total of 12.6% reported smoking ≥1 cigarette/day in early pregnancy (with none smoking ≥10 cigs/day) while only 1.3% reported consuming alcohol in early pregnancy. Mean pre-pregnancy BMI was 33.1 ± 6.6 kg/m^2 (94.8% overweight/obese) and 12.9% had a personal history of GDM. The average MET-hrs/wk in early pregnancy was 49.8 ± 22.7, with the majority expended during household (22.9 ± 14.2 MET-hrs/wk) and occupational (12.1 ± 13.2 MET-hrs/wk) activities and the lowest amount expended during sports/exercise (1.63 ± 1.86 MET-hrs/wk). The majority of this activity was light-intensity (20.3 ± 9.4 MET-hrs/wk) and only 0.2 MET-hrs/wk (±0.6) was vigorous intensity. The largest proportions of women were in the contemplation (44.2%) and preparation (37.8%) stages of change for exercise. These results are important because knowledge of demographics, health behaviors and health beliefs of inactive women at high risk for GDM is essential in informing targeted physical activity interventions designed to prevent GDM.

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AGREEMENT OF SELF-REPORTED MIGRAINE WITH INTERNATIONAL CLASSIFICATION OF HEADACHE DISORDERS-II DIAGNOSTIC CRITERIA IN A COHORT OF PREGNANT WOMEN.

*Chunfang Qiu, Michelle Williams, Sheena Aurora, Lee Peterlin, Bizu Gelaye, Ihunnaya Frederick, Daniel Enquobahrie (Center for Perinatal Studies, Swedish Medical Center, Seattle WA 98112)

Introduction: Migraine, a common neurological disorder often associated with autonomic nervous system dysfunction, has emerged as a novel risk factor for adverse perinatal outcomes including hypertensive disorders of pregnancy, preterm birth and placental abruption. Most prior studies have relied on self-report of physician-diagnosed migraine as a means for classifying pregnant women with a history of migraine. No studies have investigated the agreement of self-reported migraine with the International Classification of Headache Disorders, 2nd edition (ICHD-II) diagnostic criteria in pregnancy cohorts. Methods: Self-reported, physician diagnosed migraine was obtained in a sample of 500 women who were also interviewed using a detailed migraine questionnaire that allowed the application of ICHD-II diagnostic criteria. Results: Approximately 92% of women self-reporting a physician diagnosis of migraine received the diagnosis between the ages of 11 and 40 years. Some 6.8% of migraineurs received the diagnosis before age 10 years; 38.8% received the diagnosis between11-20 years; 42.7% between 21-30 years; 10.7% between 31-40 years; and 1.0% at age 40 or older. Approximately 81.6% of women self-reporting a physician diagnosis of migraine fulfilled ICHD-II criteria for migraine (63.1% definitive ICHD-II migraine; 18.5% ICHD-II probable migraine). In conclusion, we found excellent agreement between self-reported migraine and ICHD-II-based migraine classification in this pregnancy cohort. Conclusion: We demonstrated the feasibility of using questionnaire-based migraine assessment according to the full ICHD-II criteria in epidemiological studies of pregnant women.

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PREVALENCE AND CORRELATES OF MIGRAINE IN A COHORT OF PREGNANT WOMEN IN THE US.

*Ihunnaya Frederick, Chunfang Qiu, Daniel Enquobahrie, Sheena Aurora, Lee Peterlin, Bizu Gelaye, Michelle Williams (Center for Perinatal Studies, Swedish Medical Center, Seattle WA 98122)

Background: Migraine is a common neurological disorder of idiopathic origin, ranked among the world's leading causes of years lived with disability by the World Health Organization. The burden of migraine is highest in women of reproductive age and accumulating evidence suggest associations of migraine with increased risks of adverse perinatal outcomes including preeclampsia, fetal growth restriction and placental abruption. Methods: We characterized the prevalence, symptoms and correlates of migraine and other headaches in a cohort of 500 pregnant women attending prenatal care clinics in the Pacific Northwest. Migraine and other headache disorder were defined using the International Classification of Headache Disorders-II (ICHD-II) criteria. Assessments of headache-related disability before and during pregnancy were assessed using the MIDAS questionnaire. Logistic regression was conducted to estimate odds ratios (OR) and 95% confidence intervals (95% CI) for factors associated with migraine. Results: The lifetime prevalence of migraine was 20.0% (95% CI 16.6-23.8%). When probable migraine was included, the lifetime prevalence of migraine in this population increased to 29.8% (95% CI 25.9-34.0%). An additional 16.6% (95% CI 13.5-20.2%) of the cohort were classified has having non-migraine headaches. Migraine headaches were associated with a family history of headache or migraine (OR = 3.40; 95% CI 2.11-5.49), childhood carsickness (OR = 7.79; 95% CI 4.37-13.87), pre-pregnancy overweight/obesity status (OR = 2.12; 95% CI 1.28-3.49), and a high frequency of fatigue (OR = 2.06; 95% CI 1.13-3.76). Approximately 26.2% of migraineurs endorsed moderate or severe headache-related disability during early pregnancy. Conclusion: Migraine and headache-related disability are prevalent conditions among pregnant women.

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MATERNAL PRE-PREGNANCY SMOKING AND RISK OF SPONTANEOUS ABORTION.

*Audrey Gaskins, Stacey Missmer, Janet Rich-Edwards, Jorge Chavarro (Harvard School of Public Health, Boston MA 02115)

The few studies of pre-pregnancy smoking with risk of spontaneous abortion (SAB) are inconsistent. We prospectively examined the relation between pre-pregnancy smoking status, duration, intensity, initiation, cessation, and risk of SAB in 21,706 women between 1990-2009 in the Nurses Health Study II. Pregnancies were self-reported, with case pregnancies lost spontaneously at <20 weeks gestation and comparison pregnancies ending in ectopic pregnancy, induced abortion, or live birth. We fit multivariable log-binomial regressions using generalized estimating equations. Among the women (mean age = 31 yrs, 93% Caucasian, 29% past/current smokers), 40,075 pregnancies were reported of which 7,435 (18.6%) ended in SAB. Compared with those who had never smoked, the multivariate relative risk (RR) of SAB was 1.28 (95% confidence interval [CI] 1.15, 1.43) for current smokers and 1.03 (95% CI 0.96, 1.10) for past smokers. The association between current pre- pregnancy smoking and SAB risk was consistent across gestational length with a multivariate RR of 1.27 (95% CI 1.04, 1.55) for early first trimester SAB (<8 weeks), 1.28 (95% CI 1.06, 1.55) for late first trimester SAB (8-11 weeks), and 1.57 (95% CI 1.22, 2.03) for early second trimester SAB (12-19 weeks). Within both past and current smokers, there was no increased risk of SAB for women who smoked more frequently or smoked for longer duration. Within past smokers, there was no gradation in risk according to years since quitting smoking. Compared to never smokers, women who began smoking at young ages (<15 yrs) had a 13% (95% CI 2%, 26%) higher risk of SAB regardless of whether they still smoked. In conclusion, being a current smoker prior to pregnancy and initiating smoking at a young age were associated with increased risk of SAB.

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LABOR ABNORMALITIES, BIRTH DEPRESSION, AND SIGNS OF BRAIN INJURY IN THE PATHWAY TOWARDS CEREBRAL PALSY IN TERM BIRTHS: A MATCHED CASE-CONTROL STUDY IN MICHIGAN.

*Qing Li, Nigel Paneth, Steven Korzeniewski, Matthew Francis, Madeleine Lenski (Department of Epidemiology and Biostatistics, Michigan State University, East Lansing MI 48824)

The association between asphyxia and cerebral palsy (CP) has been investigated for more than a hundred years. Ellenberg and Nelson (2012) have criticized the non-specificity in identifying birth asphyxia in study design, and proposed separating brain injury (BI) from labor abnormalities (LA). Our study aims to investigate roles of LA, birth depression (BD), and signs of BI in the pathway towards CP in term births. This matched case-control study included children aged 2-15 who were born in Michigan. Cases were recruited from specialty clinics in 3 cities. Community controls were matched on year of birth, sex, and at least 37 gestational weeks. Using information from birth certificates, hospital discharge files and maternal interview, LA were defined as a group of factors possibly related to interruption of oxygen supply and/or blood flow during the immediate perinatal period. BD was defined as having an APGAR score of 5 or less at 5 minutes of life. BI included birth injury, neonatal seizures, encephalopathy, or assisted ventilation. McNemar's Test, conditional logit model analyses, and unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Among 90 cases and 90 controls, CP was not associated with LA (OR: 1.1; 95% CI 0.4-2.9; p = 0.81). However, CP was marginally associated with BD (OR: 5; only cases in five discordant pairs had exposure, p = 0.03, after correction for continuity p = 0.07) and significantly with BI (OR: 3.6; 95% CI 1.3-9.7; p = 0.007). After including BD, the magnitude of association between BI and CP was reduced (OR 2.4; 95% CI 0.8-6.8; p = 0.10). Analyses stratified by CP subtypes revealed a significant association between BI and quadriplegic CP (OR: 5.0; 95% CI 1.1-22.8; p = 0.04). Term births with BD and BI, but not LA, were associated with increased risk of CP. Our findings may warrant further investigation of the implications of exposure classifications and the relevance of other potentially confounding factors.

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AN ECOLOGIC LEVEL EXAMINATION OF THE RELATIONSHIP BETWEEN DENGUE AND POOR BIRTH OUTCOMES USING TIME-SERIES METHODS. *Eleanor Friedman, Emily Harville, Pierre Buekens, Kay Thomashek, Aidsa Rivera, Michael Johansson, Wanda Llovet Diaz, Yolanda Viera Maldonado (Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans LA 70118)

Previously reported risks for women who are pregnant and contract dengue include an increased risk of preterm labor. Dengue infection could result in preterm birth through several biologic mechanisms, including inflammatory cytokine release and maternal fever. We examined the possible relationship between dengue virus infections and poor birth outcomes in Puerto Rico at the ecologic level. Using time-series methods the relationship between dengue and poor birth outcomes was analyzed as rates (linear regression) and as counts (Poisson regression). The outcomes of preterm birth (PTB), low birthweight (LBW), and small for gestational age (SGA) were examined in relation to the amount of dengue at the week of birth, one week prior to birth, and two weeks prior to birth. Using rates and after adjusting of confounders, only results for PTB were statistically significant, showing a negative correlation with the rate of dengue for the week of birth (regression coefficient = -0.00552 (<0.0001)), and a positive correlation for the week before birth (regression coefficient = 0.00593 (<0.0001)). Using counts both the number of PTB and LBW were positively correlated with the number of dengue cases at the week of birth (regression coefficient = 0.0009 (<0.0001), 0.0007 (0.0142)). No other results were statistically significant. The contradictory results between rates and counts is thought to be due to the extreme seasonality associated with births in Puerto Rico, resulting in a false positive association between the counts of poor birth outcomes and dengue in Poisson models which do not correct for the changing number of births over time. The results of the rate models are surprising, and indicate that at least on a large population level, the amount of dengue is higher the week before preterm birth, but lower in the week when preterm birth occurs. Individual level analyses would be required to confirm these findings.

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THE IMPORTANCE OF ADJUSTING FOR SEASONALITY WHEN EXAMINING BIRTH DATA OVER TIME. *Eleanor Friedman, Emily Harville, Pierre Beukens, Kay Thomashek, Aidsa Rivera, Michael Johansson, Wanda Llovet Diaz, Yolana Viera Maldonado (Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans LA 70118)

Previous research has identified that poor birth outcomes, such as preterm birth (PTB), low birthweight (LBW), and small for gestational age (SGA) are associated with season of conception and birth. This study examines the effects of using poor birth outcome data that has strong seasonal components both with and without correction for the underlying seasonality of births. Data from an ecologic study on the relationship between poor birth outcomes and dengue transmission in Puerto Rico was used. Two methods of time series analysis were used, adjusted linear regression methods which controlled for seasonality in births by creating rates of poor birth outcomes as well as controlling for autoregressive errors and non-stationary data; and Poisson regression, which only controlled for the autoregressive errors and non-stationary data. The relationship between dengue and poor birth outcomes was examined at the week of birth, one week prior to birth, and two weeks prior to birth. Using rates and after adjusting of confounders, only results for PTB were statistically significant, showing a negative correlation with the rate of dengue for the week of birth (regression coefficient = −0.00552 (<0.0001)), and a positive correlation for the week before birth (regression coefficient = 0.00593 (<0.0001)). Using counts both the number of PTB and LBW were positively correlated with the number of dengue cases at the week of birth (regression coefficient = 0.0009 (<0.0001), 0.0007 (0.0142)). The contradictory results seen between rates and counts is most likely due to the extreme seasonality associated with births in Puerto Rico. For Poisson models that did not correct for the changing number of births over time, a false positive association between the counts of poor birth outcomes and dengue was seen, indicating the importance of consideration of the season in data examined over time.

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THE CONTRIBUTION OF ATTENUATED SELECTION IN UTERO TO SMALL-FOR-GESTATIONAL-AGE (SGA) BIRTH AMONG TERM AFRICAN AMERICAN MALE INFANTS. Julia Goodman, *Deborah Karasek, Elizabeth Anderson, Ralph Catalano (School of Public Health, University of California, Berkeley CA 94720)

Background: Rates of small-for-gestational-age (SGA) among term infants have declined over time, but are persistently higher among African American women than non-Hispanic white women. While higher levels of cumulative life stress and prenatal stress reported by African American women are often cited as drivers of adverse birth outcomes, mechanisms of this pathway are less clear. The racial disparity in rates of SGA combined with increased ambient stressors among African Americans would appear to contradict theories of selection in utero, which posit that natural selection conserves mechanisms allowing women to spontaneously abort gestations least likely to yield fit offspring. Small gestational size has been proposed as an indicator of fitness observable by maternal biology. Previous research suggests that exposure to ambient stress in utero results in more "culling" of small fetuses and therefore lower rates of SGA among live births. The literature on the embodiment of cumulative stress suggests mechanisms that may reconcile selection in utero with endemically high levels of SGA among African American infants. This paper tests whether attenuation of the stress response among highly stressed African American women, as suggested by the weathering hypothesis, may help to explain this apparent inconsistency. Methods: We apply time-series modeling to over 2 million African American and non-Hispanic white male term births in California over the period of January 1989 through December 2010. We test for the parabolic (i.e., "U" shaped) relationship, implied by an attenuated stress response, between unusually strong labor market contraction and the rate of SGA among African American term male infants, and a linear relationship among non-Hispanic whites. Results: We find the hypothesized parabolic relationship among term male African American infants. As expected, we find a negative linear relationship between unexpected layoffs and the rate of SGA among term male non-Hispanic whites. We estimated a 10% increase in the odds of SGA among term African American male infants born 21 weeks following maternal exposure to very high levels of unexpected layoffs. These results are robust to sensitivity analyses. Conclusion: These results may help to explain the high rates of SGA among term male African American infants, despite greater maternal exposure to ambient stress during pregnancy.

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THE CAUSAL EFFECT OF RED BLOOD CELL FOLATE ON GENOME-WIDE METHYLATION IN CORD BLOOD: A MENDELIAN RANDOMIZATION APPROACH. *Alexandra M Binder, Karin B Michels (Department of Epidemiology, Harvard School of Public Health, Boston MA 02115)

Investigation of the biological mechanism by which folate acts to affect fetal development can inform appraisal of expected benefits and risk management. This research is ethically imperative given the ubiquity of folic acid fortified products in the US. Considering that folate is an essential component in the one-carbon metabolism pathway that provides methyl groups for DNA methylation, epigenetic modifications provide a putative molecular mechanism mediating the effect of folic acid supplementation on neonatal and pediatric outcomes. In this study we use a Mendelian Randomization (MR) approach to assess the effect of red blood cell (RBC) folate on genome-wide DNA methylation in cord blood. Site-specific CpG methylation within the proximal promoter regions of approximately 14,500 genes was analyzed using the Illumina Infinium Human Methylation27 BeadChip for 50 infants from the Epigenetic Birth Cohort at Brigham and Women's Hospital in Boston. Using methylenetetrahydrofolate reductase genotype as the instrument, the MR approach identified 7 CpG loci with a significant (mostly positive) association between RBC folate and methylation level. Among the genes in closest proximity to this significant subset of CpG loci, several enriched biologic processes were involved in nucleic acid transport and metabolic processing. Compared to the standard ordinary least squares regression method, our estimates were demonstrated to be more robust to unmeasured confounding. To the authors' knowledge, this is the largest genome-wide analysis of the effects of folate on methylation pattern, and the first to employ MR to assess the effects of an exposure on epigenetic modifications. These results can help guide future analyses of the causal effects of periconceptional folate levels on candidate pathways.

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THE IMPACT OF SERUM ANTI-MüLLERIAN HORMONE ON FOLLICULAR PHASE LENGTH IN PREMENOPAUSAL WOMEN.

*Kerri Kissell, Michelle Danaher, Enrique Schisterman, Neil Perkins, Karen Schliep, Katherine Ahrens, Lindsey Sjaarda, Jean Wactawski-Wende, Sunni Mumford (NICHD, Rockville MD 20852)

Serum anti-Müllerian hormone (AMH), a well-established biomarker of ovarian reserve, reflects continuous non-cyclic growth of small ovarian follicles. AMH decreases with age, markedly so as a woman approaches menopause. Peri-menopausal lengthening of the menstrual cycle has been attributed to elongation of the follicular phase, while the luteal phase is thought to remain constant as it is dependent on corpus luteum function. This study evaluated the relationship between AMH concentrations and follicular phase length in 259 healthy premenopausal women aged 18-44 years from Buffalo, New York (2005-2007). Menstrual cycles (N = 509) were timed by ovulation prediction kits and serum samples were collected during menses, mid-follicular phase, peri-ovulation (3 times) and throughout the luteal phase (3 times), for ≤ 8 samples per cycle for 2 cycles. Average cycle-specific AMH was calculated for each woman and categorized into tertiles [<1.87 ng/mL (low), 1.87–4.30 (medium), > 4.30 (high)]. We used a linear mixed effects model to assess the effect of AMH on average follicular phase length, adjusting for age. Women in the lowest AMH tertile had the shortest follicular phase length (14.2 days, 95% confidence interval (CI): 13.5, 14.9) compared to women in the medium tertile (15.3 days, 95% CI: 14.7, 15.9) or highest tertile (17.3 days, 95% CI: 16.4, 18.1). Our study demonstrates a positive correlation between AMH and follicular phase length regardless of age. Further research investigating whether AMH alone, or in combination with other biomarkers, influences follicular phase is warranted.

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EXCESSIVE GESTATIONAL WEIGHT GAIN IS LINKED TO MID-LIFE OBESITY.

*Jeremy Coyle, David Rehkopf, Alison Cohen, Irene Headen, Barbara Abrams (University of California, Berkeley School of Public Health, Berkeley CA 94720)

Weight gain during pregnancy may contribute to the development of obesity. A meta-analysis found that excessive gestational weight gain, as defined by the 2009 Institute of Medicine guidelines, is associated with increased weight later in life. We used data from 4202 mothers from the National Longitudinal Survey of Youth 1979 cohort to assess the effect of excessive gestational weight gain in their first pregnancy on obesity at age 40. We used the Super Learner estimation algorithm and a simple substitution estimator to estimate the reduction in obesity associated with a hypothetical intervention to prevent all instances of excessive gestational weight gain in the first pregnancy (the mothers would instead gain weight consistent with the IOM recommendation). This is the attributable risk of gestational weight gain for mid-life obesity. We also analyzed this effect in various strata to determine if its magnitude varied by subpopulation. We found that intervening to eliminate excessive gestational weight gain is associated with a reduction in the prevalence of obesity by 2.4% (95% CI: 0.8-2.8%). We found evidence of interaction between this effect and a woman's age at first birth and race. The estimated effect in women whose first birth occurred at age 30 or later (0.9%; 95% CI: -1.2-1.2%) was significantly smaller than the effect in women whose first birth occurred before age 20 (3.4%; 95% CI: 1.3-4.5%) and women whose first birth occurred between ages 20 and 29 (2.4%; 95% CI: 0.5-3.1%). The effect in African American women (3.0%; 95% CI: 2.0-5.5%) was significantly larger than the effect in Caucasian women (2.2%; 95% CI: 0.3-2.5%). Neither African American or Caucasian women had an effect significantly different from that in Hispanic women (3.3%; 95% CI: 0.8-4.8%). These findings suggest that interventions to prevent excessive gestational weight gain are important for long-term obesity outcomes, especially for older and African American mothers.

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DIAGNOSIS OF AMNIOTIC FLUID INFECTION PRIOR TO CERCLAGE USING GLUCOSE AND GRAM STAIN: AN INDIVIDUAL PATIENT META-ANALYSIS.

*Yasser Sabr, Sarka Lisonkova, K S Joseph (University of British Columbia, Vancouver BC Canada)

Objective: Success of a rescue cerclage in the second trimester of pregnancy depends on the absence of subclinical microbial invasion of the amniotic cavity (MIAC). We carried out a study to assess the diagnostic performance of Gram stain and glucose concentration for the detection of subclinical MIAC. Methods: We used individual-level information from published studies on amniotic fluid (AF) culture, Grams stain and glucose tests among women with preterm labour. We calculated sensitivity, specificity, and other indices for the Gram stain test, the glucose test (≤14 mg/dl) and their combination. Logistic regression was performed to estimate the probability of infection using both tests as predictors. Model calibration ability, risk-stratification capacity and classification accuracy were evaluated. Results: The rate of culture confirmed MIAC was 11.2% (34 of 288 women). The Gram stain test had a sensitivity of 65% and a specificity of 99%. Testing positive with the Gram stain or glucose tests yielded a sensitivity of 88% and a specificity of 87%. Combining both Gram stain and glucose tests yielded a sensitivity of 62% and a specificity of 100%. Logistic regression showed that the use of both tests provided enhanced calibration ability, risk-stratification capacity and classification accuracy as compared with the use of the Gram stain test alone. Conclusion: AF Gram stain combined with glucose testing provides superior performance for the diagnosis of subclinical MIAC as compared with Gram stain testing alone. Diagnostic amniocentesis using these tests should be part of the evaluation of women considering cerclage to prolong pregnancy

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MODELING THE CIRCADIAN RHYTHM OF PRETERM LABOR ONSET AND PRETERM PREMATURE RUPTURE OF MEMBRANE IN A SAMPLE OF PERUVIAN WOMEN.

*Miguel Angel Luque Fernandez, Bizu Gelaye, Qiu Chunfang, Cande V Ananth, Sixto E Sanchez, Sonia Hernandez-Diaz, Michelle A Williams (Harvard School of Public Health, Boston MA 02215)

Background & Objective: There are conflicting reports regarding circadian variation in the onset of spontaneous labor (sPTL) and preterm premature rupture of membranes (PPROM) leading to spontaneous preterm births (sPTB). We modeled participant reported time of sPTL and PPROM onset leading to sPTB. Methods: We used multiple parametric and non-parametric methods including trigonometric regression and piecewise cubic splines in generalized linear models to model the circadian variation in sPTL and PPROM onset among 476 women with singleton pregnancies in Lima, Peru. Subgroup analyses were performed according to selected maternal and newborn characteristics. Results: A statistically significant morning peak was seen among all sPTB and this was similar for births preceded by sPTL or PPROM. A clear aggregation of SPTL and PPROM onset was noted between 6-10am (42% of cases) with a smaller peak between 5-10pm. The patterns of sPTL and PPROM onset were similar across groupings of gestational age at delivery, fetal gender, parity, maternal pre-pregnancy weight, educational attainment and maternal age. Discussion: Circadian rhythms modulate physiologic processes and the timing of several medical disorders, including cortisol and oxytocin secretion, myocardial infarction, stroke, and even time of death. The biological rhythm of sPTL and PPROM onset appears to be aligned with the diurnal variation in cortisol secretion. Greater understanding of circadian rhythms in pregnancy and parturition may yield important insights into the pathophysiologic processes underlying the mechanisms of preterm births.

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NON-INVASIVE VENTILATION (NIV) AND MORTALITY IN PATIENTS WITH A FIRST-TIME ACUTE ADMISSION FOR A COPD EXACERBATION: A NATIONWIDE STUDY. *Sandra Soegaard Toettenborg, Reimar Wernich Thomsen, Henrik Nielsen, Soeren Paaske Johnsen, Ejvind Frausing Hansen, Peter Lange (University of Copenhagen - Department of Public Health, Copenhagen Denmark)

Background: A Cochrane review found non-invasive ventilation (NIV) to reduce mortality in patients with a COPD exacerbation. In 2008, a national COPD quality program (DrCOPD) was initiated to monitor treatment in all COPD patients including increase the use of NIV in Danish hospitals. Now, NIV is recommended in addition to medical treatment for patients admitted to Danish hospitals with an exacerbation and concurrent hypercapnic respiratory failure. Aim: We examined subsequent national and regional trends in the use of NIV and trends in all-cause mortality among patients admitted with a COPD exacerbation. Methods: We did a population-based prospective study using data from DrCOPD and the Danish National Patient Register to identify all first-time hospitalizations with COPD from 2008 to 2011 (n = 24,982) and use of NIV during hospitalization. Date of death was retrieved from the Danish Civil Registration System. Results: NIV increased during the four years of follow-up (age, sex, and co-morbidity adjusted relative risk (RR)1.21, 95% CI 1.05; 1.38), but with considerable regional variation. The use of NIV in combination with mechanical ventilation also increased (RR 1.36, 95% CI 1.03; 1.80). Nationally, all-cause in-hospital-, and 6-months mortality decreased from 5.8% to 5.1%, and 19% to 17.8%, respectively. 30-day mortality increased from 7.4% to 9%, with some variation between regions. Conclusion: The present study shows a substantial improvement in the use of NIV and NIV in combination with mechanical ventilation in all regions of Denmark following the initiation of a national COPD quality improvement program in 2008. Variations between regions should be addressed by Danish Regions. Given the mortality reducing properties of NIV found in clinical trials, we can hypothesize that concurrent reductions in mortality could stem from higher use of NIV. Further investigation is warranted.

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INCOME AS AN EFFECT MODIFIER IN THE RELATIONSHIP BETWEEN SMOKE-FREE CAR RULES AND CHILDHOOD ASTHMA. *Kimberly Nguyen, Shanta Dube, Brian King, David Homa, Bridgette Garrett (Office on Smoking and Health, Centers for Disease Control and Prevention, Atlanta GA 30341)

Secondhand smoke (SHS) exposure such as parental smoking among children is associated with ever having asthma, wheezing, and other respiratory diseases.[1,2,3] This study assessed the effect of income on the relationship of smoke-free car rules and childhood asthma, using landline-only data from the 2011 Behavioral Risk Factor Surveillance System; the childhood asthma module was administered in 33 states and the SHS module was administered in 3 of those states. Among households in 33 states with income <$25,000, 15.1% of children ever had asthma compared to 11.9% in >$25,000 households (Chi-square, $p < 0.0001$). In Indiana, Louisiana, and Mississippi, 40.0% of <$25,000 households with a parent who smokes and at least one child <18 years reported that smoking is allowed in the car, compared to 26.1% in >$25,000 households (Chi-square, $p < 0.0001$). Among these three states, households with incomes <$25,000 that allow smoking in the car were more likely to have children who ever had asthma (Odds Ratio [OR]: 2.2; 95%Confidence Interval [CI]: 1.2-4.2) compared to households that prohibit smoking in the car, after controlling for parental age, gender, race/ethnicity, smoking, and asthma status. No significant association was observed for households with incomes >$25,000. Effective strategies to increase adoption of smoke-free car rules are needed. [1]Burke H, Leonardi-Bee J, Hashim A, Pine-Abata H, Chen Y, Cook DG, Britton JR, McKeever TM. 2012. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. Pediatrics; 129(4):735-44. [2]Chen YC, Tsai CH, Lee YL. Early-life indoor environmental exposures increase the risk of childhood asthma. 2011. Int J Hyg Environ Health;215 (1):19-25. [3]The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General. 2006. Available at: http://www.surgeongeneral.gov/library/reports/tobaccosmoke/index.html

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RATIO OF CONTROLLER-TO-TOTAL ASTHMA MEDICATIONS IN INDIANA'S MEDICAID POPULATION. *Amy Brandt, Barbara Lucas, Champ Thomaskutty (Indiana State Department of Health, Indianapolis IN 46204)

Background: In Indiana, 9.5% of children have a current asthma diagnosis. A low ratio of controller-to-total asthma medications has been linked to lower quality of life and poor disease control. We sought to determine the percent of children with asthma with a low medication ratio in Indiana's Medicaid population, examine differences between high vs low ratio groups, and investigate associations between the ratio and health outcomes. Methods: Children (0-17) with persistent asthma were identified from Indiana's 2011 Medicaid claims data. Controller-to-total asthma medications ratio (AMR) was defined as the sum of controller prescription claims divided by the total number of controller and rescue claims. Children with an AMR of 0.5 or more were classified as high ratio and those with AMR of less than 0.5 were classified as low. Analysis included bivariate analyses and multivariate logistic regression. Results: In 2011, 18,272 Indiana children enrolled in Medicaid had persistent asthma. Of these, 9,837 (46.2%) were classified as low ratio. Sex, race and mean age differed significantly between groups with a higher proportion of low AMR children being male (60.0% v 58.3%), black (34.1% v 24.7%) and younger (mean 8.3 v 8.5 years). Low AMR children had a mean of 5.9 rescue prescriptions; high AMR children had 2.6 ($p < 0.0001$). A total of 3,318 children with persistent asthma had an asthma-related ED visit in 2011, 56.1% of which were considered low ratio. Adjusting for demographic covariates, low AMR children were 2.0 (95% confidence interval: 1.8-2.2) times more likely to have an asthma ED visit than high AMR children. Conclusions: In 2011, 46.2% of children with persistent asthma in Indiana's Medicaid population took more rescue than long-term control medications, increasing their odds of having an asthma ED visit, signifying a need for improved education and better access to primary care.

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EXPERIENCES OF RACISM AND ASTHMA INCIDENCE IN AFRICAN AMERICAN WOMEN. Patricia Coogan, *Jeffrey Yu, George O'Connor, Lynn Rosenberg (Slone Epidemiology Center at Boston University, Boston MA 02215)

Chronic stress resulting from experiences of racism may increase the incidence of adult-onset asthma through effects on the immune system and the airways. We conducted prospective analyses of the relation of experiences of racism to asthma incidence in the Black Women's Health Study, which has followed 59,000 US black women since 1995 with mailed biennial questionnaires. The present study included 38,142 women free of asthma in 1997 and followed through 2011; over follow-up 1068 women reported incident physician-diagnosed asthma together with asthma medication use. Racism scores were created from questions asked in 1997 about the frequency of everyday racism (e.g., people act as if you are dishonest) (5 questions) and of lifetime racism (i.e., unfair treatment on the job, in housing, by police). Racism was also assessed in 2009. We used Cox regression models to derive incidence rate ratios (IRR) and 95% confidence intervals (CI) for incident asthma in categories of the everyday and lifetime racism scores, adjusted for age, body mass index, smoking, and other potential confounders. For experiences of racism reported in 1997, the IRR was 1.45 (95% CI 1.19-1.78) (p for trend < 0.0001) in the highest compared to the lowest quartile of everyday racism and 1.44 (95% CI 1.18-1.75). in the highest compared to lowest category of lifetime racism. Among women who reported the same levels of racism in both 1997 and 2009, the IRRs for the highest categories of everyday and lifetime racism were 2.12 (95% CI 1.55-2.91) and 1.66 (95% CI 1.20-2.30), respectively. Our results suggest that the chronic stress associated with experiences of racism may contribute to adult-onset asthma. Because prevalence of both experiences of racism and asthma are high among US black women, the association is of public health importance.

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HETEROGENEITY IN SOCIAL CONTACT AMONG SCHOOL-AGE CHILDREN AND IMPLICATIONS FOR INFLUENZA TRANSMISSION. *Molly Leecaster, Warren Pettey, Damon Toth, Jeanette Rainey, Amra Uzicanin, Matthew Samore (University of Utah, Salt Lake City UT 84132)

Understanding transmission dynamics for acute respiratory infectious diseases relies on disease detection, pathogen properties, and information on contact behavior affecting transmission. Data on contact behavior are currently limited, especially for school-age children, and do not represent the heterogeneity in contact among elementary, middle, and high schools. Precise contact estimates can be used in mathematical models to understand infectious disease transmission and better target surveillance and intervention efforts. We report results from a study to collect social contact data on school-aged children and examine the transmission dynamics of influenza. We collected contact data for school-aged children in 19 K-12 schools from diverse demographic and climatic regions in Utah using radio signal strength indicator sensors that recorded contacts within 4 feet. We developed contact networks using sensor data, providing visualizations of contact patterns as well as numeric contact measures such as degree (number of unique contacts), distribution, and density (number of observed contacts divided by the number of possible contacts). These contact networks were used in mathematical models to evaluate differences in influenza transmission linked to heterogeneity in contact. Data from three schools, an elementary, middle, and high school, will be presented. The average density within classrooms was 0.91 for elementary schools and 0.53 for middle schools. The average density over the whole school day was 0.26 for elementary schools and 0.16 for middle schools. These contact patterns were linked to differing results from mathematical disease transmission models. Contact pattern heterogeneity should be incorporated into transmission models to better understand disease dynamics and assess implications for disease surveillance, prevention and control.

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UNDERUTILIZATION OF SPIROMETRY IN ADULTS DIAGNOSED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: WHO TO TARGET FOR IMPROVED CLINICAL MANAGEMENT? *Dana Mowls, Vinay Cheruvu, Melissa Zullo (Department of Epidemiology and Biostatistics, Kent State University, Kent OH 44242)

Spirometry, the gold standard to diagnose chronic obstructive pulmonary disease (COPD), is underutilized resulting in misdiagnosis, inappropriate drug therapy, and risk for respiratory/cardiovascular event. Understanding characteristics of adults diagnosed/not diagnosed by spirometry will permit improved clinical management. This research describes associations between adults' characteristics, comorbidity, healthcare utilization and spirometry. This was a cross-sectional study using 2011 Behavioral Risk Factor Surveillance System data. Weighted multivariable logistic regression examined factors associated with (n = 13,484) and without spirometry (n = 3,131). Spirometry was reported by 78% of adults and increased with age: compared to adults <40, those 55-64, 65-74, and ≥75 were 1.9 (95% confidence interval (CI): 1.3-2.6), 2.4 (CI: 1.6-3.6), and 2.4 (CI: 1.6-3.7) times more likely to have spirometry, respectively (trend < 0.001). Spirometry was more likely in: black (odds ratio (OR) = 2.4; CI: 1.5-3.8) compared to white non-Hispanic; current (OR = 1.4; CI: 1.1-1.8) and former (OR = 1.4; CI: 1.1-1.9) compared to never smokers; adults with asthma (OR = 2.6; CI: 2.1-3.2), depressive disorder (OR = 1.3; 1.1-1.6), cardiovascular disease (OR = 1.6; CI: 1.3-2.1), and with a doctor (OR = 1.8; CI: 1.3-2.5) compared to without; and those who had been to ER/hospital for COPD (OR = 1.3; CI: 1.1-1.7). Those less likely to receive spirometry were Hispanic (OR = 0.60; CI: 0.3-0.6) and reported exercise in the past 30 days (OR = 0.81; CI: 0.67-0.98). Adults diagnosed with COPD without spirometry were Hispanic, healthier, younger, and had less utilization. This is problematic as disease progression will occur not only due to aging and behaviors but due to suboptimal clinical management as evidenced by not having spirometry. These findings support projections that by 2020 COPD will be the 5th leading cause of morbidity and increase from the 4th to 3rd leading cause of mortality.

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RELATIONSHIP OF MATERNAL SERUM LEVELS OF ANTIOXIDANTS WITH ASTHMA IN CHILDREN IN THE UNITED STATES. *Kamal Eldeirawi (College of Nursing, University of Illinois at Chicago, Chicago IL 60612)

Introduction: Studies linking maternal serum concentrations of carotenoids with asthma in children are lacking. The objective of this study was to examine the relationships of life-time doctor-diagnosed asthma in children with maternal serum levels of beta-carotene, alpha-carotene, and beta-cryptoxanthin in a representative sample of the United States' children. Methods: This cross-sectional study analyzed data on 2290 pairs of mothers and their children aged 2 months-6 years who were examined in the third National Health and Nutrition Examination Survey (NHANES III). Bivariate and multiple logistic regression analyses were conducted treating serum concentrations of the antioxidants as categorical variables (quintiles). Results: Mothers of children with asthma had significantly lower serum concentrations of alpha-carotene, beta-carotene, and beta-cryptoxanthin than mothers of children without asthma with significant does-dependent inverse associations between serum levels of these nutrients and the odds of asthma. The odds ratios (ORs) comparing children of mothers whose serum concentrations were in the 5th quintile with children whose mothers' serum concentrations were in the 1st quintile were 2.53 (95% CI: 1.06-6.03), 3.48 (95% CI: 1.32-9.17), and 2.60 (95% CI: 1.24-5.47), for alpha-carotene, beta-carotene, and beta-cryptoxanthin, respectively, with significant tests for trends obtained for the three nutrient markers. These associations persisted after adjusting for age, sex, ethnicity, maternal smoking during pregnancy, and educational level of the family reference person. Conclusion: Our study demonstrated inverse associations of maternal serum levels of alpha-carotene, beta-carotene, and beta-cryptoxanthin with the odds of asthma in children. These findings highlight the need for longitudinal studies to further examine the relationships of maternal diet during pregnancy or early in the child's life with the risk of asthma in children.

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THE ANATOMY OF RACIAL DISPARITIES IN INFANT MORTALITY BY SPECIFIC CAUSES OF DEATH. *Abdulrahman El-Sayed, Darryl Finkton, Katherine Keyes, Sandro Galea (Columbia University, New York NY 10032)

Infant mortality among Blacks is nearly three times that of non-Hispanic Whites. Studies attempting to explain this disparity suggest that racial differences in socioeconomic position (SEP) and maternal risk behaviors may explain some, but not all, excess infant death among Blacks relative to non-Hispanic Whites. We examined the contribution of SEP and maternal risk behaviors to disparities in specific causes of infant mortality to better understand the anatomy of the Black-White infant mortality disparity. We fit a multivariable logistic regression model of infant mortality adjusted for socioeconomic and maternal behavioral risk factors. A second multivariable logistic regression model, using residuals extracted from the first model as the outcome, was fit by the interaction between race and cause of death. We compared crude Black-White mortality ratios to model-predicted residual ratios to understand the contribution of SEP and maternal risk behaviors to disparities by cause. Blacks had higher risk for infant mortality than non-Hispanic Whites in both crude (OR 2.80, 95% CI 2.71-2.89) and adjusted (1.98, 1.90-2.06) models. SEP and maternal risk behaviors explained nearly 30% of the Black-White disparity in infant mortality overall, and more than 50% of the disparity in several specific causes of infant mortality including homicide, accident, sudden infant distress syndrome (SIDS), gastrointestinal diseases, respiratory distress syndrome (RDS), and perinatal infection. Adjustment for SEP and maternal risk behaviors had little effect on disparities in other specific causes, including maternal complications of pregnancy, birth trauma, and intrauterine hypoxia or birth asphyxia. Differences in SEP and maternal risk behaviors explained a large proportion of racial disparities in causes of infant death related to preterm birth and low birth weight as well as causes occurring after birth, but did not explain differences in causes of death related to parturition. These findings help focus policy attention toward those causes most amenable to social and behavioral intervention, and research attention to those causes not explained by SEP and behavioral differences.

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PARADOX LOST: THE HISPANIC INFANT MORTALITY PARADOX OVER THE PAST TWO DECADES. *Abdulrahman El-Sayed, Magdalena Paczkowski, Sandro Galea (Columbia University, New York NY 10032)

Despite lower socioeconomic position, Hispanics in the US have been shown to have lower rates of several important population health metrics than non-Hispanic Whites, including infant mortality. This mortality advantage is particularly pronounced among infants born to foreign-born Hispanic mothers. However the literature to date has been relegated to point-in-time studies that preclude a dynamic understanding of ethnic and nativity differences in infant mortality among Hispanics and non-Hispanic Whites. Therefore, we assessed secular trends in the relation between Hispanic ethnicity, maternal nativity, and infant mortality between 1989-2006 using a linked birth-death dataset from one US state. Congruent to previous research, we found a significant mortality advantage among infants of Hispanic relative to non-Hispanic White mothers between 1989-2000. However, because of an upward trend in infant mortality among infants of Hispanic mothers after 1992—largely attributable to increasing infant mortality among infants of foreign-born mothers among them—the risk of infant mortality was higher among infants of Hispanic mothers overall compared to those of non-Hispanic White mothers after 2001. These findings suggest that the 'Hispanic paradox' with respect to infant mortality is resolving. Changing sociocultural norms among Hispanic mothers and changes in immigrant selection and immigration processes may explain these observations, suggesting directions for future research.

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ESTIMATING HEALTH-SELECTIVE MIGRATION IN PATIENTS WITH RHEUMATOID ARTHRITIS USING ADMINISTRATIVE DATA. *Jeremy Labrecque, Ryan Kyle, Sasha Bernatsky (McGill University, Montreal QC Canada)

Aim: There is great interest in the use of administrative data for the surveillance of chronic diseases. Health-selective migration, however, may have important an influence on spatial patterns of disease. We studied within province health-selective migration among rheumatoid arthritis (RA) patients in Quebec comparing migration before and after diagnosis. Methods: RA cases were identified using Quebec billing and hospitalization databases from 1999-2008. Adults over 25 years of age satisfying at least one of three algorithms were considered to have RA: two RA diagnoses by a physician at least 8 weeks but less than 2 years apart, one RA diagnosis by a rheumatologist or one hospital discharge diagnosis of RA. Forward sortation area (FSA, the first three digits of the postal code) was available for each patient updated yearly. The main variable of interest was RA and the outcome was within-province migration defined as a change in FSA from the previous year. Generalized estimating equations (GEE) were used to estimate the log-binomial model to account for the multiple observations per individual. Covariates in the model included sex, age and participation in a government drug subsidy plan and FSA-level characteristics such as socioeconomic status and urbanicity. Results: 34,915 FSA changes were observed in 650,678 person-years. There was an important interaction between age and RA yielding different risk ratios (RRs) by age. The RR for migration in RA patients post-diagnosis relative to before at 30 years was 0.81 (95% confidence interval, CI: 0.77-0.86), at 50 years 0.96 (95% CI: 0.92-0.99) and at 70 years 1.12 (95% CI: 1.08-1.17). Conclusion: These results demonstrate an important qualitative change in health-selective migration in RA patients by age. This is in contrast to previous research suggesting that people with chronic diseases move more often to be closer to care or family. Potential limitations include imperfect ascertainment of diagnoses.

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DOES EDUCATIONAL ATTAINMENT NARROW SOCIAL INEQUALITIES IN MORTALITY AFTER STROKE? COMPARING EDUCATIONAL INEQUALITIES IN STROKE-FREE AND POST-STROKE POPULATIONS. *Jessica Daniel, Paola Gilsanz, Stefan Walter, Ichiro Kawachi, M Maria Glymour (Harvard University School of Public Health, Boston MA 02115)

Background: Some evidence suggests a narrowing of social inequalities in mortality post-stroke. If this is the case, educational differences should be associated with reduced inequalities in post-stroke mortality. We compare educational differences in mortality in stroke and stroke-free populations to assess this possibility of stroke acting as an effect modifier. Methods: Health and Retirement Study (n = 20,730) participants were interviewed biennially from 1998-2010. Years of education (range 0 to 17+) was modeled as a linear spline (knots at 12 and 16 years). Strokes (3,407 events) were identified by self or proxy report. Mortality was defined as death by 2010. We used logistic regression models to estimate the effect of education on mortality in both samples, restricting to those alive in 1998 and controlling for race, age, sex, birth place, and mother's education. We estimated the absolute effects of education on mortality for a reference category: 74-year-old white males born in "central" US, with maternal education above 8 years. Results: Education was associated with similar relative reductions in mortality among both the stroke (Odds ratio [OR] per year <12 = 0.958; 95% CI: 0.910, 1.007) and stroke-free (OR per year <12 = 0.978; 95% CI: 0.953, 1.004) populations. In the stroke population, the probability of mortality for someone with: 10 years of education was 73.8%, 12 years was 67.8% (8.1% reduction compared to 10 years), and 16 years was 66.7% (9.6% reduction compared to 10 years). In the stroke-free population, the probability of mortality for someone with: 10 years of education was 69.0%, 12 years was 61.9% (10.3% reduction compared to 10 years), and 16 years was 52.9% (23.4% reduction compared to 10 years). Conclusion: The absolute reduction in mortality associated with education is larger for stroke-free adults than stroke patients. Educational inequalities in mortality are smaller among stroke patients than among the population at large.

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SOCIAL CAPITAL AND SLEEP DISTURBANCES: DOES THE WORKPLACE MATTER? *Tuula Oksanen, Paula Salo, Jaana Pentti, Mika Kivimäki, Jussi Vahtera (Finnish Institute of Occupational Health, Turku Finland)

Sleep problems are increasingly common among working populations. Emerging evidence shows the importance of workplace social capital (i.e. social cohesion, trust, and reciprocity in the workplace) to employee health, although its association with sleep remains unknown. To investigate the issue, we used data from 48,094 Finnish public sector employees in over 3000 work units who responded to at least two consequtive surveys between 2000 and 2012. Survey responses to a psychometrically tested 8-item measure of workplace social capital in 2000-02, 2004 and 2008 were aggregated to work unit level using an ecometrics approach.This approach accounts for the nesting of social capital items within individuals and includes the work unit level in the analysis, resulting in a three-level model. From this model, we estimated work unit-level residuals, adjusted for individual covariates, for each work unit. We added these residuals to the grand mean of each survey to constitute the workplace social capital measure. Self-reported sleep disturbances were evaluated with Jenkins Sleep Problem Scale in 2004, 2008, and 2012. Additionally, data on purchases of sleep medicine were obtained from pharmacy records during the 2 years following the assessment of workplace social capital. We applied binomial logistic regression analysis by the generalised estimating equations to model serial measurements of workplace social capital, time-dependent health-related covariates, and sleep disturbances. Of the participants, 26% reported sleep disturbances and 6% used sleep medicines during the follow-up. Adjusted for socio-demographics, a 1-unit increase in workplace social capital decreased the risk of self-reported sleep disturbances by 11% and the use of sleep medicine by 13%. Further adjustments for health-related factors only slightly attenuated the associations. These new findings suggest that high workplace social capital is beneficial for sleep.

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THE "MISSING LEVEL" PROBLEM IN MULTILEVEL STUDIES: EVIDENCE THAT CROSS-CLASSIFIED MULTILEVEL MODELS ARE PREFERRED TO TRADITIONAL MULTILEVEL MODELS.

*Erin Dunn, Tracy Richmond, Carly Milliren, S.V Subramanian (Massachusetts General Hospital, Boston MA 02114)

Background: Multilevel modeling approaches are now widely used to study the effect of hierarchical phenomenon on individual health and behavior. However, most multilevel analyses only examine one level of influence (e.g., neighborhoods), missing potentially other relevant levels of importance (e.g., schools). In this study, we examined the role of schools and neighborhoods on adolescent smoking behavior, using both traditional multilevel and cross-classified multilevel models, in order to better understand the effect of this "missing level" problem. Methods: Data came from the National Longitudinal Study on Adolescent Health (n = 16,553). Smoking status was defined as the number of cigarettes smoked in the past 30 days. We conducted two separate sets of multilevel models, one for neighborhoods, defined by census tracts (n = 2,278) and one for schools (n = 128). In the cross-classified model, we simultaneously modeled the effect of both schools and neighborhoods. Results: In the multilevel analysis of schools, we found that 6.3% of the variability in smoking was accounted for differences between schools. In the multilevel analysis of neighborhoods, 5.1% of the variability was due to differences between neighborhoods. In models that adjusted for individual-level covariates (age, sex, race, socioeconomic status), we found the school (2.01) and neighborhood multilevel models (1.57) had similar variance estimates. However, in the cross-classified model, the variance estimate for school (2.12) was much greater than neighborhoods (0.034). Conclusions: Results of this study suggest that the "missing level" problem may be a serious concern for epidemiological studies using traditional multilevel models. Findings from this study suggest that cross-classified multilevel models are a more appropriate method to account for and model the clustering of individuals in the multiple hierarchical settings to which they are embedded.

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SOCIOECONOMIC STATUS AND TRAJECTORY OF OBESITY FROM BIRTH TO CHILDHOOD: THE EARLY CHILDHOOD LONGITUDINAL STUDY-BIRTH COHORT.

*Jessica Jones-Smith, Marlowe Dieckmann, Laura Gottlieb, Jessica Chow, Lia CH Fernald (Johns Hopkins Bloomberg School of Public Health, Baltimore MD 21205)

Objective: We used longitudinal data from a US nationally representative birth cohort to test whether the odds of obesity during the first 6 years of life differed according to socioeconomic status (SES). Methods: Using six waves of data from the Early Childhood Longitudinal Study-Birth Cohort (n = 5,000), we examined the odds of obesity according to age, socioeconomic status, and race/ethnicity. We defined obesity as body mass index (BMI) z-score >2 standard deviations (SD) above the WHO Childhood Growth Standard reference mean. We used a composite index (using income, education, and occupation) of socioeconomic status. We implemented generalized estimating equation (GEE) models to estimate SES-specific trajectories of the odds of obesity. We tested whether any SES-obesity relation varied significantly according to race/ethnicity. Results: The relationship between socioeconomic status and obesity varied significantly by race/ethnicity. Obesity was clearly associated with socioeconomic status among whites, Hispanics and Asians; the adjusted odds of obesity began to diverge according to SES after the first 9 months of life and by approximately 4 years, children with the highest SES had a significantly lower odds of obesity, which persisted until the end of the study (age 5-6) (Odds Ratio (95% Confidence Interval): 0.47 (0.30, 0.73); 0.28 (0.14, 0.59); 0.41 (0.19, 0.89), for highest SES quintile compared to lowest at 5 years among whites, Hispanics and Asians, respectively). SES was not significantly related to obesity among African Americans and American Indians during early childhood. Conclusions: SES was associated with obesity among more ethnic groups (whites, Hispanics, and Asians) than previously reported. SES-based risk for obesity begins early in life among these race/ethnic groups, which implies that efforts aimed at preventing these disparities will be relevant during these early childhood years.

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DOES INCOME INEQUALITY GET UNDER THE SKIN? DEPRESSION, ANXIETY AND MENTAL DISORDERS IN SAO PAULO, BRAZIL.

*Alexandre Chiavegatto Filho, Ichiro Kawachi, Maria Carmen Viana, Wang Yuan-Pang, Laura de Andrade (School of Public Health, University of Sao Paulo, Sao Paulo SP Brazil)

Income inequality has been associated with a variety of health issues. On the other hand, the mechanisms by which it affects health are still unknown. We aimed to test the original income inequality theory, by analyzing its association with depression, anxiety and mental disorders. We analyzed a sample survey of 3,542 individuals aged 18 years and older living in the Sao Paulo Metropolitan Area. Presence of depression, anxiety and any mental disorder was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Bayesian multilevel logistic models were performed to test the association of income inequality (measured by the Gini coefficient) and mental health, after controlling for demographic and socioeconomic characteristics. Living in medium and high inequality areas was statistically associated with increased risk of depression, relative to low inequality areas (Odds Ratio: 1.76; 95% Credible Interval: 1.21-2.55, and OR: 1.53; 95% CI 1.07-2.19, respectively). The same was not true for anxiety (OR: 1.25; 95% CI: 0.90-1.73 for medium, and OR: 1.07; 95% CI: 0.79-1.46 for high). In the case of any mental disorder, the results were mixed, being statistically significant for medium (OR: 1.32; 95% CI: 1.03-1.68), and marginally significant for high inequality areas (OR: 1.24; 95% CI: 0.97-1.57). In general, our findings were consistent with the income inequality theory, i.e. people living in places with higher income inequality had an overall higher odd of mental disorders, albeit not always statistically significant. The fact that depression, but not anxiety, was statistically significant could indicate a pathway by which inequality influences health, as depression has been frequently conceptualized as a "backward-looking" emotion. In this case, living in highly unequal areas may lead poor individuals to develop feelings of failure, both in life and work, when they compare themselves to their richer neighbors.

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PERSISTENT SPATIAL CLUSTERING OF CERVICAL CANCER INCIDENCE IN OHIO: A MULTILEVEL AND SPATIAL APPROACH.

*Jesse Plascak, Catherine Calder, Electra Paskett (The Ohio State University, Columbus OH 43210)

Cervical cancer disparities have persisted in areas of decreased socioeconomic status (SES) and healthcare access. Spatial analyses of individual- and group-level factors were used to better understand relationships between space, place and cervical cancer incidence in Ohio. Cases diagnosed between 1996 and 2009 were from Ohio's population-based cancer registry. Controls were from RTIs synthetic population dataset (RTI Press, 2009(10):905). County (chlamydia rate, teen birth rate, percent < 65 years without health insurance); school district (childhood poverty rate, land value per pupil) and census tract (median household income, percent unemployed, percent impoverished, percent < high school degree) data were gathered from the University of Wisconsin's County Health Rankings, Ohio Department of Education and the U.S. Census Bureau. Principal component analysis of SES-related census tract variables yielded a single SES component capturing 70% of the original factors' variance. Odds ratios (OR) and 95% confidence intervals were estimated from multilevel logistic regression models. Group-level residual spatial clustering of null (random intercept only) and final models was assessed using Moran's I. Percent uninsured, teen birth rate and childhood poverty were positively associated, and SES, land value and chlamydia rates were negatively associated with cervical cancer. Final model covariates accounted for much of the spatial clustering observed in null models. The significantly elevated odds of cervical cancer (ORs 1.23-1.50) among 5 of Ohio's 6 largest city school districts resulted in (non-significantly) reduced odds (ORs 0.81-0.96) upon final model covariate adjustment. This approach has reinforced known associations involving traditional SES factors, and demonstrated new associations and patterns related to non-traditional SES factors measured at the school district level. Further research is needed investigating these school district SES factors.

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ECONOMIC CONDITIONS AND HEALTH BEHAVIORS DURING THE "GREAT RECESSION". *Sam Harper, Thomas Charters, Erin C Strumpf, S Jody Heymann, Arijit Nandi (McGill University, Montreal QC Canada)

The adoption of healthier behaviors has been hypothesized as a mechanism to explain recent empirical findings of population health improvements during economic downturns. We estimated the effect of the local unemployment rate on health behaviors using pooled annual surveys from the 2003-2010 Behavioral Risk Factor Surveillance Surveys, population-based telephone surveys of the US adult general population. Analyses were based on approximately 1 million respondents aged 25 or older living in 90 Metropolitan Statistical Areas and Metropolitan Divisions (MMSAs). The primary exposure was the quarterly MMSA-specific unemployment rate, and we used fixed effects for MMSA and quarter to identify the causal effect of variations in unemployment. Outcomes included alcohol consumption, smoking status, attempts to quit smoking, body mass index, overweight/obesity, and past month physical activity or exercise. The average unemployment rate across MMSAs increased from a low of 4.5% in 2007 to a high of 9.3% in 2010. In multivariable models accounting for individual-level socio-demographic characteristics and MMSA and quarter fixed effects, a one percentage-point increase in the unemployment rate was associated with 0.153 [95% confidence interval (CI) = -0.311, 0.005] fewer drinks consumed in the past month and a 0.143 (95% CI = -0.281, -0.004) percentage-point decrease in the prevalence of past-month heavy drinking; these effects were driven primarily by men. Changes in the unemployment rate were not consistently associated with other health behaviors. Although individual-level unemployment status was associated with higher levels of alcohol consumption, smoking, and obesity, the effects of the recession were largely invariant across individual-level employment groups. Our results do not support the hypothesis that health behaviors mediate the effects of economic conditions on mortality.

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YOUTH WHO ENGAGE IN FIRST TIME SEX UNDER THE INFLUENCE: SEXUAL VALUES AND SOCIAL PRESSURES. *Lilian Ghandour, Faysal El Kak, Rola Yasmine (American University of Beirut, Beirut Lebanon)

This study examined the sexual values and communication patterns of young people who reported using alcohol/drugs during their first sexual experience (oral, anal and/or vaginal). An online survey on sexual behaviors, attitudes, and perceptions was conducted in 2012 among private university students (N = 2543) from Lebanon. About 11% (n = 104) of students who reported being sexually active (n = 943) recounted having been using alcohol/drugs at sexual debut. Substance use during sex debut was at least twice more likely in males, non-Arab foreigners, those living independently, and the somewhat to not-at-all religious or spiritual [p-values <0.01]. Students who had attended a religious private high school, always lived in Lebanon, and were currently in a relationship were 40-60% less likely to report substance use at sex debut [p-values <0.01]. Indirect communication with a partner on one's preference in sexual activity was twice more likely among those who had sexual debut while under the influence. Students who talked to a paternal guardian (Odd ratio, OR = 1.75, p = 0.013) or friend (OR = 3.9, p = 0.009) about sexual issues were also at higher odds of substance use during first-time sex. The latter were also more likely to believe that their peers took drugs or alcohol a lot before having sex (OR = 5, 95% CI = 2.1-10.0) adjusted for gender, nationality, relationship status, having lived abroad, and religiosity. Youth that engaged in sex debut under the influence were also more likely to agree that there is pressure to have sex by a certain age (OR = 2.2, 95% CI = 1.35-3.57), that it is fun to sexually experiment with strangers (OR = 2.7, 95% CI = 1.69-4.54) and that it is boring to have the same sexual partner for a longtime (OR = 1.96, 95% CI = 1.21-3.21). This picture of risk enhancing communication, peer pressure, and desire of sexual exploration highlights an urgent need to instill sexuality education among youth, in their home and schools settings.

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JOHN HENRYISM, IMMIGRATION, ACCULTURATION AND RISK OF HYPERTENSION AMONG HISPANICS: FINDINGS FROM THE WICER STUDY. *Bernadette Boden-Albala, Eric Roberts, Leigh Quarles (Mount Sinai School of Medicine, New York NY 10029)

Hispanics have similar prevalence of hypertension (HT) compared to non-Hispanic whites yet experience higher stroke incidence; disparities are particularly stark between Caribbean Hispanics and Whites in Northern Manhattan. Little is known regarding the social determinants of HT in this population. This study examines the association between John Henryism (JH) and education with HT in a cohort of Hispanics from Northern Manhattan. The WICER study is an ongoing population based cohort study aiming to explore the social determinants of vascular disease. Logistic models assessed the joint effect of JH and education on the odds of HT adjusting for confounders. Three-way interactions assessed whether nativity, language(s) used, and time in the community modified the effect of JH-education on HT. Our sample is 889 Hispanics, mean age = 49, 69% female, 52% have less than a high school education, 86% are immigrants, 80% only speak Spanish at home, and 18% have been in the community for fewer than 6 years. In logistic models replicating Sherman James' work we observe similar odds of having HT among persons with high JH irrespective of educational achievement. When we stratify by language used at home we find that persons that speak only Spanish have a prevalence of HT of approximately 30% irrespective of reported level of JH and educational achievement. Among persons that do not only speak Spanish we observe a patterning of results closer to James' original findings – persons with high JH and low education have a much higher prevalence of HT (52%) compared to individuals with high JH and high education (32%). Interactions for nativity and time in the community were not significant. A higher percent of more acculturated persons endorse above average scores of JH (46% vs 59%) suggesting JH may hold less explanatory power among recent immigrants. Additionally, the low prevalence of HT among less acculturated persons may be a result of the healthy immigrant effect.

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THE IMPACT OF RESIDENTIAL REHABILITATION ON INJECTION DRUG USE IN BALTIMORE, MARYLAND, 2000-2011. *Sabriya Linton, Gregory Kirk, Shruti Mehta (Johns Hopkins Bloomberg School of Public Health, Baltimore MD 21205)

Aims: Despite the growth of studies connecting poor neighborhood conditions with drug use, few studies have assessed the impact of neighborhood revitalization on drug use. This study sought to assess the relationship between neighborhood residential rehabilitation and injection drug use. Methods: Individual level data from a cohort of injection drug users in Baltimore, Maryland was linked to neighborhood data, from 2000-2011. Cross-classified multilevel models were used to assess the association between neighborhood residential rehabilitation, defined as the percentage of residential properties where investment in maintenance exceeded $5,000 USD, and injection drug use over time. We also assessed whether relocating between neighborhoods of varying levels of residential rehabilitation impacted injection drug use. Residential rehabilitation was categorized into 3 groups; the 1st category had the lowest residential rehabilitation. Results: After adjusting for neighborhood economic deprivation and individual-level covariates, residence in a neighborhood in the 2nd category of rehabilitation, as compared to residence in a neighborhood in the 1st category, was associated with a 19% reduction in injection drug use [Adjusted Odds Ratio (AOR) = 0.81; 95% Confidence Interval (CI) = 0.71,0.92], and residence in a neighborhood in the 3rd category of rehabilitation was associated with a 22% reduction in injection drug use [AOR = 0.78; 95% CI (0.64,0.96)]. The protective impact of rehabilitation was observed among persons who remained in neighborhoods with high rehabilitation, those who relocated within or between neighborhoods of high rehabilitation, and those who relocated from neighborhoods with low rehabilitation to neighborhoods with high rehabilitation. Conclusion: This study suggests that residential rehabilitation may reduce the likelihood of injection drug use. Additional studies are needed to understand the mechanisms behind this relationship.

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SOCIAL DISPARITIES IN SELF-REPORTED SLEEP HABITS IN A POPULATION-BASED SAMPLE. *Elizabeth Suarez, Andre Araujo (New England Research Institutes, Inc., Watertown MA 02472)

It is recognized that sleep problems increase risk for adverse cardiometabolic outcomes. We examined the social patterning of sleep in relation to race/ethnicity and socioeconomic status (SES). Data were obtained from 4,144 men/women aged 31-87y who participated in the Boston Area Community Health (BACH) Survey (2008-10), a racially/ethnically diverse population-based survey. Outcomes including self-reported sleep duration, sleep latency (time to fall asleep), restless sleep, and sleep apnea (Berlin questionnaire) were modeled using multivariable linear and logistic regression adjusted for age, sex, race/ethnicity, SES, self-rated health, physical activity, BMI, medication use, alcohol use, smoking, and stress/anxiety. The sample was 27.1% black, 12.5% Hispanic, 60.5% white with mean(SE) age 52.6(0.5)y. Mean sleep duration and latency were 6.63h and 16.5min, 20.7% reported <6h sleep/night, 35.3% reported restless sleep, and 28.4% had sleep apnea. There were no significant 2-way interactions between sex, race/ethnicity, and SES. In adjusted logistic models, Hispanic subjects were twice as likely to report <6h sleep/night than whites (OR = 2.2, 95% CI: 1.2-4.0), with no differences between black/white subjects or by SES. Sleep apnea or restless sleep did not vary by race/ethnicity or SES. In adjusted linear models, black subjects slept 24min less than white subjects, with no differences between Hispanic/white subjects or by SES. Time to fall asleep was 30% and 26% higher among black and Hispanic subjects vs. white subjects. Subjects with low and medium SES required 48.2% and 34.6% more time to fall asleep than subjects with higher SES. Given the known influence of sleep on cardiometabolic risk, these differences in sleep parameters (sleep duration and latency) could widen social disparities in key public health indicators. Grant Support: R21MD006769, U01DK05684.2

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INTERPERSONAL DISCRIMINATION AND DEPRESSIVE SYMPTOMATOLOGY: EXAMINATION OF SEVERAL PERSONALITY-RELATED TRAITS AS CONFOUNDERS IN A CROSS SECTIONAL STUDY OF RACIAL/ETHNIC HETEROGENEOUS ADULTS. *Haslyn Hunte, Katherine King, Margaret Hicken, Hedwig Lee, Tene Lewis (Purdue University, West Lafayette IN 47907)

Although the precise mechanism of depression is unknown, it is widely believe that perceived discrimination, a hypothesized daily stressor, is one of the many factors that are involved in the onset of a depressive disorder. However, because personality dispositions may magnify the impact of daily stressors, the uncertainty associated with reports of discrimination continues to be a methodological concern. As such, we examined if, and to what extent, hostility, anger repression and expression, pessimism, optimism and self-esteem confounds the relationship between perceived discrimination and CESD-based depression symptoms in a racial/ethnic heterogeneous probability-based sample of community-dwelling adults (N = 3,105). We used multivariable ordinary least squares regression analyses controlling for several sociodemographic characteristics. Hostility, anger repression, pessimism and self-esteem were significant confounders of the relationship between discrimination and depression, accounting for approximately 38% of the total effect (beta: 0.1892, $p < 0.001$) between the two. However, discrimination remained a positive predictor of depression symptoms (beta: 0.1176, $p < 0.001$). These results are noteworthy for several reasons. First, this study is among the first to characterize confounding effects of more than two personality-related traits between discrimination and depression symptoms. An additional strength of this study is the generalizability of the results, given that we used a representative, multi-ethnic sample of community dwelling adults, unlike previous studies.

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CORD BLOOD LEAD AND MANGANESE AND NEONATAL BEHAVIOR. *Sharon Sagiv, J Kevin Nugent, T Berry Brazelton, David Bellinger, Chitra Amarasiriwardena, Susan Korrick (Boston University School of Public Health, Boston MA 02118)

Prenatal and early life exposure to heavy metals can adversely impact neurodevelopment with resulting cognitive and behavioral impairments in childhood and beyond. Less is known about the impact of these exposures on early infant behavior. We examined the association between prenatal exposure to lead and manganese and neonatal behavior in a large prospective birth cohort of 788 mother-newborn pairs recruited at birth between 1993 and 1998 in New Bedford, MA. Cord serum lead and manganese levels were quantified with inductively coupled plasma-mass spectrometry and behavior was assessed for 542 infants approximately 2 weeks after the birth using the Neonatal Behavioral Assessment Scale (NBAS). The NBAS is a test of the infant's behavioral capacities, including responsiveness to visual or auditory stimuli, motor tone and activity, and state regulation, with scores ranging from 1 (worst) to 9 (best). Median (range) cord serum lead and manganese levels were 1.3 (0-9.4) μg/dL and 4.0 (0.2-22.2) μg/dL, respectively. Multivariable models included adjustment for proxies of socioeconomic status such as maternal education, race, marital status, and income. We estimated inverse associations between cord serum lead and manganese and NBAS measures of alertness with, e.g., reductions in quality of alertness scores of -0.4 (95% CI: -0.9, 0.1) and -0.5 (95% CI: -1.0, -0.1) for the highest compared with the lowest quartile of cord lead and manganese, respectively. Associations with other behavioral capacities, including state- and motor-related domains, were less consistent. These results provide suggestive evidence for associations between prenatal exposure to metals and early measures of neonatal behavior, particularly alertness. Identifying modifiable risk factors for adverse behavior, as well as sensitive tests of neuropsychological function in early infancy, could allow for earlier intervention, which may be important for promoting healthy neurodevelopment.

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ASSOCIATION BETWEEN EXPOSURE TO LEAD IN SOILS AND PRETERM BIRTH IN MEDICAID WOMEN IN SOUTH CAROLINA. *Harley Davis, Jihong Liu, Marjorie Aelion, Bo Cai, James Burch, Suzanne McDermott (University of South Carolina Department of Epidemiology and Biostatistics, Columbia SC 29208)

Preterm birth, defined as birth at <37 weeks of gestation, is a significant public health problem, in the United States (US) and in South Carolina (SC), with 2009 prevalence rates of 12.9% and 14.5%, respectively. Environmental exposure to lead (Pb) has been implicated in preterm birth. However, no studies have examined this association in a high-risk Medicaid population. We conducted a multilevel analysis to examine the association between environmental exposure to Pb in soils and preterm births. Soil samples were taken from 11 areas in SC, analyzed for total Pb (in mg/kg), and concentrations were kriged at the geocoded addresses of mothers enrolled in SC Medicaid and giving birth from 1996-2001 (n = 8,664). Demographics and risk factors were obtained from SC birth certificates, Medicaid billing records and Census 2000 data. We found that the odds of having a preterm birth was 1.24 times higher among women living in areas with the highest quartile of Pb in soils (>72.0 mg/kg) as compared to those in the lowest quartile of Pb (<12.49 mg/kg); odds ratio (OR) = 1.24 and 95% confidence interval (CI): 1.05, 1.55. After adjusting for individual level factors, the odds of having a preterm birth was higher among those in the highest Pb quartile (OR = 1.65, 95% CI: 1.11, 2.46) and in the second highest Pb quartile (38.3-72.0 mg/kg; OR = 1.56, 95% CI: 1.03, 2.34). Further adjustment of both individual and neighborhood level factors did not change this association. Both maternal race, and a neighborhood being predominately black, were associated with preterm birth in the model with individual and neighborhood risk factors, suggesting a racial disparity in preterm birth in this population. Overall, after adjusting for well-known preterm birth risk factors, higher concentrations of Pb were associated with preterm birth in Medicaid women, suggesting environmental exposures in soils should be considered as a risk factor for preterm births in this population.

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A LONGITUDINAL STUDY OF FINE PARTICULATES AND RISK OF PRETERM BIRTH IN CONNECTICUT 2000-2006. *Gavin Pereira, Kathleen Belanger, Michelle Bell (Yale School of Public Health, New Haven CT 06511)

Preterm birth is a leading cause of perinatal mortality and morbidity, occurring among almost 13% of neonates in the United States. Few studies have examined the effect of ambient fine particulate matter (PM2.5) on risk of preterm birth and it is uncertain as to whether results were affected by individual predisposition, such as genetic factors or social conditions that might vary considerably between women. We addressed this uncertainty by testing the hypothesis that a woman is more at risk of preterm labor when her pregnancies have elevated exposure to ambient PM2.5, comparing pregnancies to the same woman. This study included women who gave birth by vaginal delivery in Connecticut 2000-2007 to at least two singleton live born neonates without congenital anomaly, living within 10km of an air quality monitor (N = 27,804 women, N = 58,331 births). Analyses were conducted using conditional logistic regression, matching pregnancies to the same women. Adjustment was made for covariates that change between pregnancies: parity, maternal age and smoking. The adjusted odds ratios (OR) per inter-quartile range (IQR) increase in PM2.5 in first trimester (IQR 3.25 μg/m3), second trimester (IQR 3.25 μg/m3), third trimester (IQR 3.77 μg/m3), and whole pregnancy (IQR 2.19 μg/m3), were OR 1.11 (95% CI 1.11, 1.21), OR 0.93 (95% CI 0.85, 1.02), OR 1.08 (95% CI 0.99, 1.18), and OR 1.11 (95% CI 0.99, 1.24). In this study, pregnancies with elevated PM2.5 exposure were more likely to result in preterm birth than other pregnancies to the same women at lower levels of exposure.

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EXPOSURE TO AMBIENT COURSE PARTICULATE MATTER BY GESTATIONAL PERIOD AND AUTISM SPECTRUM DISORDERS IN NORTH CAROLINA AND CALIFORNIA. *Amy E Kalkbrenner, Gayle C Windham, Marc L Serre, Yasuyuki Akita, Xuexia Wang, Brian P Thayer, Julie L Daniels (University of Wisconsin-Milwaukee, Milwaukee WI 53201)

Recent studies suggest that traffic-related air pollutants, including particulate matter (PM), are associated with autism spectrum disorder (ASD) in California (CA). We examined whether this association held in new data from CA and an area with different air pollutant patterns: North Carolina (NC). Children with an ASD were identified by records-based surveillance (n = 645 born in central NC in 1994, 96, 98, and 2000, and n = 334 born in the San Francisco area in 1996) compared to randomly sampled children born in the same counties and years from birth records (12,435 in NC and 2,232 in CA). Exposure to course PM (PM_{10}) at the birth address was assigned to each child using a geostatistical method, interpolating in space and time using daily concentrations from air pollution regulatory monitors, then averaging by trimester of pregnancy. We used generalized additive models to estimate odds ratios (OR) and 95% confidence intervals for a 10 $\mu g/m^3$ increase in PM_{10}, parametrically adjusting for birth year, state, maternal education and age, race/ethnicity, neighborhood-level urbanicity and median household income, and including non-parametric (LOESS) terms for birth month to account for seasonal trends. Temporal patterns in PM_{10} were pronounced, with inverse correlations between the 1st and 3rd trimester concentrations (r = -0.72), but none with the 2nd trimester. Adjusted ORs for trimesters 1 – 3 were: 0.87 (0.76, 1.01), 0.98 (0.83, 1.15), and 1.38 (1.15, 1.66); and after simultaneously including 1st and 3rd trimester concentrations to account for the inverse correlation, were: 1st trimester: 1.03 (0.82, 1.29) and 3rd trimester: 1.42 (1.06, 1.90). Our study adds to previous work showing a relationship between traffic-related air pollutants and ASD, with results consistent with increased susceptibility in the 3rd trimester; although greater PM_{10} misclassification in the 1st trimester may contribute to results, given address changes between then and birth.

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A REPEATED-MEASURES STUDY OF RECREATIONAL WATER EXPOSURE, NON-POINT SOURCE POLLUTION, AND RISK OF ILLNESS. *Cynthia J Lin, Chris D Heaney, Timothy J Wade, Rachel T Noble, Steve Wing (Gillings School of Global Public Health, University of North Carolina, Chapel Hill NC 27599)

Discharge of stormwater runoff onto beaches is a major cause of beach closings and advisories in the United States. Prospective studies of recreational water quality and health have often been limited to two time points (baseline and follow-up). Little is known about the risk of illness from repeated seasonal water exposure. We conducted a repeat-measures study to examine the risk of illness associated with regular water exposure that could be potentially affected by stormwater runoff in the northern Outer Banks of North Carolina. We enrolled adult surf instructors and lifeguards in the summer, 2011 and followed them for an average of 7 weeks (maximum = 14). Participants (n = 38) provided daily reports of water exposure (e.g., swimming, head immersion, swallowing water) and self-reported illness symptoms (gastrointestinal, upper respiratory, ear, skin, eye) on weekly follow-up surveys. To assess exposure to fecal contamination, we measured enterococci and recorded daily precipitation and time since a storm event. We used conditional fixed-effects logistic regression to compare within-person variation of illness to water activities, precipitation, and enterococci levels. Compared to having no water exposure, water exposure in the presence of any enterococci (adjusted odds ratio, aOR = 1.65; 95% confidence interval, 95% CI 0.82-3.34) appeared to increase the odds of any illness on the same day more than in the absence of any enterococci (aOR = 1.08; 95% CI 0.52-2.25). Any swimming in the antecedent 2 days was also associated with an increased odds of any illness (aOR = 1.71; 95% CI 1.11-2.62). Ocean exposure and enterococci were associated with illness in workers with regular water exposure. Additional analyses will evaluate time lags between exposure and illness. This abstract does not necessarily reflect EPA policy.

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COUNTY-LEVEL ENVIRONMENTAL QUALITY AND ASSOCIATIONS WITH INDIVIDUAL- AND COUNTY-LEVEL PRETERM BIRTH. *Lynne Messer, Kristen Rappazzo, Jyotnsa Jagai, Danelle Lobdell (Portland State University, Portland OR 97207)

Human health is influenced by simultaneous exposure to stressors and amenities, but research usually considers single exposures. We constructed a county-level Environmental Quality Index (EQI) using principal components analysis with data from five domains (air, water, land, built, sociodemographic). With data from the National Center for Health Statistics (2002; n = 3,989,704), we report associations among rural-urban stratified, domain-specific and overall indices for preterm birth (PTB) odds to mothers in the United States. Race-stratified linear regression estimated prevalence differences (PD(95% confidence interval(CI))) in county-level rates of PTB (n = 3141) for quintiles of index exposure. Fixed slope, random intercept multilevel logistic models estimated odds ratios (OR(95% CI)) for index quintiles and individual PTB. Results differed by domain, racial group, and urbanicity. Increasing quintiles of the air index were associated with increased ORs and PDs for PTB (e.g., 5th quintile OR = 1.21(1.16, 1.27); PD = 0.020(0.013, 0.026) versus 1st quintile). In the most urban counties, an inverse relationship between the sociodemographic domain index and PTB (e.g., 5th quintile, OR = 0.70(0.66, 0.74); PD = -0.041(-0.048, -0.034)) was observed but in the 3 less urban strata positive associations were noted (suburban strata 5th quintile, OR = 1.29(1.19, 1.40); PD = 0.028(0.020, 0.037)). Generally, results for county-and individual-level analysis followed similar patterns, but not consistently so. The EQI, land, water, and built indices had mixed results with PTB for both county-and individual-level analyses. This work allows us to consider both associations with cases and with rates of PTB. The EQI quantifies environmental burden faced by counties while domain specific indices inform policy makers about the primary stressors in the county. These environments appear linked to both individual and county-level outcomes. This abstract does not reflect EPA policy.

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USING PROBABILISTIC BIAS ANALYSIS TO ASSESS POSSIBLE SELECTION BIAS IN A CASE-CONTROL STUDY. *Xin Cui, Onyebuchi A Arah, Beate Ritz (University of California, Los Angeles, Fielding School of Public Health, Los Angeles CA 90095)

We are conducting a population-based case-control study on the effects of ambient pesticide exposures on Parkinson's disease (PD) in three rural agricultural counties in central California. Population-controls were recruited from tax assessor residential parcels and enrolled during an in-person visit. Based on 360 PD cases and 394 controls, we previously reported an increased PD risk for those with combined residential exposures to ziram, maneb, and paraquat (Odds Ratio: 1.86; 95% Confidence Interval: 1.09, 3.18), pesticides implicated in neurodegeneration by animal and cell models. Due to the low participation rate (~50%) among eligible controls and our ability to assess exposures at all addresses independent of participation, we evaluated whether selection bias could explain our findings. Our study employs a geographic information system derived pesticide exposure assessment model that does not rely on participants' recall and generates exposure estimates at all selected addresses, allowing us to conduct probabilistic bias analysis. Using data on all controls who were eligible and either agreed or refused to participate, we conducted unconditional logistic regression analyses. For bias analysis, we modeled selection probabilities using factors that might have affected selection such as age, race and gender relying on associations observed among participants and external information for selected residences from the census and nearest enrolled neighbors. We used Monte Carlo simulations for the bias analysis. This probabilistic bias analysis with data on study participants is providing realistic insights into potential impact of selection bias. We outline the assumptions needed to explain whether and how our previous findings could be affected by selection bias due to low control participation rates.

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THE EFFECT OF ATMOSPHERIC PARTICULATE MATTER ON SURVIVAL OF BREAST CANCER AMONG US FEMALES. *Xiaohui Xu, Hui Hu, Amy B Dailey, Haidong Kan (University of Florida, Gainesville FL 32606)

Background: Short term effects of ambient particulate matter (PM) on cardiopulmonary morbidity and mortality have been consistently documented. However, no study has investigated its long term effects on breast cancer survival. Methods: We selected all female breast cancer cases (n = 285,106) available from both the California Surveillance Epidemiology and End Results cancer data and daily monitoring PM10 and PM2.5 data in each county in California obtained from U.S. Environmental Protection Agency from 1999-2009, United States to investigate the effect of PM on breast cancer survival. Results: Results from Kaplan-Meier survival analysis show that female breast cancer cases with higher exposures to PM10 and PM2.5 had a significant shorter survival than those with lower exposures ($p < 0.0001$). The results from Cox Proportional-Hazards models suggest that exposure to higher PM10 (HR: 1.14, 95% CI: 1.12-1.16, per 10 μg/m3) or PM2.5 (HR: 1.44, 95% CI: 1.41-1.47, per 5 μg/m3) was significantly associated with early mortality among female breast cancer cases after adjusting for demographic factors, cancer stage and year diagnosed. Interactions between cancer stage and PM were also observed; the survivals of patients with earlier cancer stages were more likely impacted by exposure to PM. Conclusions: This study suggests that exposure to high levels of PM may have deleterious effects on the length of survival from breast cancer among females. The findings from this study warrant further investigation.

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GASTROINTESTINAL SYMPTOMS AMONG SWIMMERS FOLLOWING RAIN EVENTS AT A BEACH IMPACTED BY URBAN RUNOFF. *Timothy J Wade, Reagan R Converse, Elizabeth A Sams, Ann H Williams, Edward Hudgens, Alfred P Dufour (EPA, Research Triangle Park NC 27711)

Gastrointestinal symptoms among swimmers have been associated with fecal contamination at beach sites impacted by discharges of human sewage. Rainfall and storm water runoff can transport pollutants, including fecal contaminants, into beach water. We investigated the association between diarrhea among swimmers and rain events at a beach in South Carolina impacted by stormwater runoff. During the summer of 2009, we enrolled and interviewed 11,159 beachgoers. We obtained information about swimming exposures and we then contacted them by telephone 10-12 days later to ascertain the incidence of diarrhea (3 or more loose stools in a 24 hour period) and other symptoms. Rainfall was measured using an on-site rain gauge. There was at least some rainfall within the previous 24 hours (1-day lag) and within the 24-48 hours (2-day lag) for 12 and 14 of the 29 study days, respectively. Rainfall was classified as none; low-moderate (≤0.39 inches); or high (>0.4 inches, 90th percentile). Unadjusted incidence of diarrhea was 3.0%, 4.0%, 4.4%, and 6.5% among non-swimmers; swimmers (body-immersion) following no rainfall in the previous 24 hours; swimmers following low-moderate rainfall and swimmers following high rainfall, respectively. Adjusted Odds Ratios and 95% Confidence Intervals compared to non-swimmers were: 1.33(0.95-1.86); 1.55(1.07-2.25); and 2.14(1.32-3.48) for swimmers with no rainfall, low, and high rainfall in the prior 24 hours, respectively. There was also a significant trend across categories among swimmers ($p = 0.003$). Rainfall the day of swimming and during the 24-48 hour lag were not as consistently associated with diarrhea. In conclusion, diarrhea among swimmers was associated with rainfall in the 24 hours prior to swimming at a beach impacted by urban runoff. This abstract does not reflect EPA policy.

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EARLY CHILDHOOD LEAD EXPOSURE AND EDUCATIONAL OUTCOMES: APPLICATION OF CAUSAL INFERENCE MODELS. *Sheryl Magzamen, Michael Amato, Pamela Imm, Marty S Kanarek, Colleen F Moore (University of Oklahoma Health Sciences Center, Oklahoma City OK 73102)

Early childhood lead exposure has been associated consistently with neurocognitive impairment, traditionally measured by intelligence quotient testing, and more recently, by performance on school-based end-of-grade (EOG) exams. Race/ethnicity and socioeconomic status are strongly related lead exposure, as well as strongly related to school achievement, thus complicating the identification of the causal effect of lead exposure on educational outcomes. To address this issue, we implemented a point-treatment marginal structural model (MSM) to assess the causal relation between early childhood lead exposure and reading proficiency categories in the Wisconsin Childhood Lead Levels and Educational Outcomes (CLLEO) Study. A total of 1,109 students who were tested for blood lead levels (BLL) before age three consented to have results from the 4th grade Wisconsin Knowledge and Concepts Exam (WKCE) provided to the study. Children were considered exposed if 10mcg ≤BLL ≤19mcg and unexposed if BLL < 5mcg. Race, parent education, parent employment, insurance status, household characteristics and comorbid conditions were self-reported by parents or guardians on a mailed survey. In traditional logistic association models, children with lead exposure had significant increased odds of not meeting reading proficiency levels of the WKCE (Odds Ratio: 2.02, 95% CI: 1.29, 2.92). Using the point treatment MSM, the odds ratio for low reading proficiency given lead exposure was 5.56 (95% CI bootstrapped estimates: 0.59, 8.889.) However, the causal estimate may be subjected to residual confounding, due to the temporality assumptions necessary for the correct identification of the treatment model. These findings may have important implications for educational and housing policy.

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HOUSEHOLD ORGANOPHOSPHORUS PESTICIDE USE AND PARKINSON'S DISEASE. Shilpa Narayan, Zeyan Liew, Kimberly Paul, Pei-Chen Lee, Janet S Sinsheimer, Jeff M Bronstein, *Beate Ritz (Department of Epidemiology, University of California, Los Angeles CA 90095)

Background: Household pesticide use is widespread in the United States. Since the 1970s, organophosphorus chemicals (OPs) have been common active ingredients in these products. Parkinson's disease (PD) has been linked to pesticide exposures but little is known about the contributions of chronic exposures to household pesticides. Here we investigate whether long-term use of household pesticides, especially those containing OPs, increases the odds of PD. Methods: In a population based case-control study, we assessed frequency of household pesticide use between ages $16 \leq 45$ years for 357 cases and 807 controls relying on the California Department of Pesticide Regulation product label database to identify ingredients in reported household pesticide products and the Pesticide Action Network pesticide database of chemical ingredients. Using logistic regression we estimated the effects of household pesticide use. Results: Frequent use of any household pesticide increased the odds of PD by 39% [odds ratio (OR) = 1.39 (95% confidence interval (CI): 1.06, 1.83)]; frequent use of products containing OPs increased the odds of PD more strongly by 82% [OR = 1.82 (95% CI: 1.26, 2.63)] and frequent organothiophosphate use more than doubled the odds of PD. Sensitivity analyses showed that estimated effects were independent of other pesticide exposures (ambient and occupational) and the largest odds ratios were estimated for frequent OP users who were carriers of the 192QQ paraoxonase genetic variant related to slower detoxification of OPs. Conclusions: We provide evidence that household use of OP pesticides is associated with an increased risk of developing PD.

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SOLAR UV RADIATION AND CHILDHOOD CANCER. *Christina Lombardi, Julia Heck, Myles Cockburn, Beate Ritz (Fielding School of Public Health, UCLA, Los Angeles CA 90095)

Background: Studies have shown that higher solar ultraviolet radiation exposure (UVR) may be related to lower risk of some cancers in adults. Recently a large ecological study reported lower risks of some cancers among children living in higher UVR cities and countries. In a large population-based case-control study in California we tested the hypothesis that specific childhood cancers may be influenced by UVR. Methods: Cancers in children ages 0 to 5 years were identified from California Cancer Registry records for 1986-2007 and linked to birth certificate data. Controls – frequency matched by year of birth – were sampled from the birth certificates at a ratio of 20:1. Based on the birth address, we assigned UVR exposure in units of Watt-hours/m^2 to subjects using a geostatistical exposure model developed with data from the National Solar Radiation Database. Results: For cases with UVR exposure of 5111 Watt-hrs/m^2 or above we estimated a reduction in odds of developing acute lymphoblastic leukemia (Odds ratio (OR): 0.89, 95% CI:0.81, 0.99), hepatoblastoma (OR: 0.69, 95% CI: 0.48, 1.00), and non-Hodgkin's lymphoma (OR: 0.71, 95% CI: 0.50, 1.02) adjusting for mother's age, mother's race and child's year of birth. Conclusions: Our findings suggest that UVR during pregnancy may decrease the odds of some childhood cancers. Future studies should explore additional factors that may be correlated with UVR exposure, investigate trimester-specific effects and possibly include biomarkers of immune function and vitamin D to investigate possible pathways for the observed associations.

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DIETARY EXPOSURE TO POLYCHLORINATED BIPHENYLS AND RISK OF MYOCARDIAL INFARCTION IN WOMEN – A POPULATION-BASED PROSPECTIVE COHORT STUDY. Charlotte Bergkvist, Marika Berglund, Alicja Wolk, *Agneta Åkesson (Karolinska Institutet, Stockholm Sweden)

Background: Fish, especially fatty fish, may promote cardiovascular health. The role of major food contaminants, such as polychlorinated biphenyls (PCBs), present in fish remains however to be explored. We assessed the association between dietary exposure to PCBs, proposed to play a role in the etiology of cardiovascular disease, and risk of myocardial infarction in women. Methods: In the population-based prospective Swedish Mammography Cohort, 33,446 middle-aged and elderly women, free from cardiovascular disease, cancer and diabetes at baseline (1997) were followed through 2009. Based on a detailed questionnaire on diet and lifestyle factors, we estimated the dietary exposure to PCB-153 (an indicator of total PCBs in food) and the intake of long-chain omega-3 fish fatty acids (eicosapentaenoic acid and docosahexaenoic acid, EPA and DHA). The estimated PCB exposure via foods, based on a large recipe-based database, showed reasonable validity against several PCB-biomarkers. Incidence of myocardial infarction was ascertained through linkage to national registers. Results: During 12 years of follow-up (387,539 person-years), we ascertained 1,386 incident cases of myocardial infarction. Women in the highest quartile of PCB exposure (median 286 ng/day), had multivariable-adjusted relative risk (RR) 1.20 (95% confidence interval (CI), 1.00-1.43) of myocardial infarction compared to lowest (median 101 ng/day). The RR increased (1.57, 95% CI, 1.10-2.24) after further adjustments for EPA and DHA intake. In mutually adjusted models, PCB exposure was associated with a clear dose-dependent increased risk, while the intake of EPA and DHA was associated with a decreased risk. Conclusion: Exposure to PCBs via diet was associated with increased risk of myocardial infarction.

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THE IMPACT OF NEIGHBORHOOD TRAFFIC DENSITY AND DEPRIVATION ON LUNG FUNCTION AMONG CHILDREN WITH ASTHMA. *Sara L Gale, John Radke, Michael Jerrett, Alan E Hubbard, Ira B Tager (School of Public Health, University of California, Berkeley, Berkeley CA 94704)

To investigate the extent to which traffic exposure affects the lung function of children with asthma and how local neighborhood factors may modify this relation, a merge of epidemiologic, environmental health and geographic methods is necessary. The Fresno Asthmatic Children's Environment Study (FACES) is a longitudinal cohort study of children with asthma in Fresno, California that followed participants from 2000-2008 to explore short-term and long-term effects of ambient air pollution on lung function (as measured by spirometry). With publicly available data on traffic counts in Fresno, CA from 2000-2008, we built a spatial model of traffic exposure with kernel density methods that varies both temporally and spatially for the FACES cohort. To capture and quantify neighborhood characteristics, we constructed individual neighborhoods based on global positioning software (GPS) data and walking distances around participant homes. To assess the marginal risk difference of lung function among children with asthma exposed to high levels of traffic pollution and those exposed to lower levels of traffic pollution (as measured by traffic density), we apply semi-parametric, causal inference methods and use Targeted Maximum Likelihood Estimation (TMLE). The marginal change in lung function from exposure to high neighborhood traffic to lower neighborhood traffic, without stratification for neighborhood deprivation, is -0.233 (95% CI -0.338, -0.129). The results can be interpreted as–the average decrease of FEV1 is 0.233 L, or there is a 12% reduction in lung function. Either neighborhood deprivation does not modify the effect of traffic on lung function or there is not enough data to evaluate this type of effect modification. The findings indicate that neighborhood exposure to traffic adversely affects lung function among the FACES cohort of children with asthma.

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INTEGRATING AIR POLLUTION EXPOSURE WITH A MODEL OF SOCIOECONOMIC VULNERABILITY AND BIRTH OUTCOMES.

*Ayaz Hyder, Keita Ebisu, Petros Koutrakis, Kathleen Belanger, Michelle Bell (Yale University, New Haven CT 06514)

Adverse birth outcomes maybe associated with socioeconomic and environmental vulnerability. This study tested the vulnerability-capacity model of population health using low birth weight (LBW, weight <2500g), preterm birth (PTB, gestational age <37 weeks) and small for gestational age (SGA, <10th percentile for gestational age and gender). This model hypothesizes that: 1) there is greater variability in the outcome at a point in time between neighborhoods that are characterized by vulnerability and 2) there is greater variability in the outcome over time within neighborhoods that are characterized by vulnerability. Birth certificate data from Connecticut (2000-2006) provided annual proportion for each outcome at the census tract-level. Measures of vulnerability were obtained from the Census data (e.g., median household income, % adults with less than high school education) Gestational exposure was calculated using calibrated and processed satellite-based predictions of particulate matter <2.5 µm (PM2.5). Average PM2.5 exposure for all births within a tract measured environmental vulnerability. To examine study hypotheses, statistical methods were used to calculate measures of variability, test for heteroscedasticity, and visual plots. Initial results indicated support for the first hypothesis in some but not other birth outcomes. For the first hypothesis, in 2000, measures of variability in LBW, SGA, and PTB had interquartile range/mean = 1.12, 1.01, 0.80, range/mean = 7.90, 6.16, 3.51, and coefficient of variation = 89%, 80% and 63%, respectively. The test for heteroscedasticity was significant for LBW and SGA with all measures of socioeconomic vulnerability, for LBW and PM2.5 exposure, and for PTB and % unemployed. We observed no support for the second hypothesis. These results showed that vulnerability (socioeconomic and environmental) may be driving population-level patterns in some adverse birth outcomes. Other outcomes may require a more complex model.

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USING SATELLITE- AND MONITOR-BASED DATA TO ASSESS THE RELATIONSHIP BETWEEN PM2.5 EXPOSURE AND BIRTH OUTCOMES IN CONNECTICUT AND MASSACHUSETTS (2000-2006).

*Ayaz Hyder, Hyung Joo Lee, Keita Ebisu, Petros Koutrakis, Kathleen Belanger, Michelle Bell (Yale University, New Haven CT 06510)

Background: Air pollution may be related to adverse birth outcomes. Exposure is often based on land-based monitoring stations but this approach suffers from limited spatial coverage. Satellite data offer an alternative data source for exposure assessment. Methods: We used birth certificate data on births in Connecticut and Massachusetts, U.S. (2000-2006). Gestational exposure to PM2.5 was estimated from monitoring data (EPA) and satellite data. Satellite data were processed and modeled, under different methods (Satellite(1) and Satellite(2)), before exposure assessment. Regression models related birth outcomes with PM2.5 exposure while controlling for several confounders. Birth outcomes evaluated were change in birth weight for term birth (BW), term low birth weight (TLBW, <2500g), small for gestational age (SGA, <10th percentile for gestational age and gender), and preterm birth (PTB, <37 weeks). Results: Overall, the exposure assessment method modified the magnitude of the effect estimates of PM2.5 on birth outcomes. Change in BW per inter-quartile range (2.41 µg/m3) increase in PM2.5 (95% CI) was -6.2 (-7.9, -4.6), -15.7 (-20.5, -10.8) and -19.0 (-23.0, -14.9), using the Monitor, Satellite(1) and Satellite(2) methods, respectively. Adjusted odds ratio (aOR), under Monitor, Satellite(1) and Satellite(2) methods, for TLBW were 1.01 (0.98-1.04), 1.06 (0.97-1.16), and 1.08 (1.01-1.16); for SGA were 1.03 (1.01-1.04), 1.06 (1.03-1.10) and 1.08 (1.04-1.11); and for PTB were 1.00 (0.99-1.02), 0.98 (0.94-1.03) and 0.99 (0.95-1.03). Conclusions: Our study is among the first to use satellite imagery for health effects studies. We found a significant association between PM2.5 and birth outcomes (BW, SGA) under different exposure assessment methods.

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COMPARISON OF PROSPECTIVELY AND RETROSPECTIVELY ASSESSED CAFFEINE CONSUMPTION IN A PRE-CONCEPTION COHORT.

*Christina A Porucznik, Kyley J Cox, Lindsey C Schmidt, Joseph B Stanford (University of Utah School of Medicine, Division of Public Health, Salt Lake City UT 84108)

We assessed caffeine exposure prospectively and thrice retrospectively in a cohort of Utah women, ages 18-44, trying to conceive. Participants charted cervical fluid to identify an estimated day of ovulation or conception (EDO/C) and completed an exposure assessment on EDO/C+2 days (i.e. the day after she recognized EDO/C). Retrospective assessments were performed at three times corresponding to typical times at which participants may be enrolled into case-control studies during pregnancy: 1) EDO/C+18 days, early pregnancy recognition, 2) EDO/C+6 weeks, first prenatal visit, and 3) EDO/C +38 weeks, delivery. The exposure assessment captured quantity and frequency of caffeine consumed from beverages and other sources. Caffeine contents were determined using the U.S. Department of Agriculture Nutrient Database for Standard Reference and used to create a summary estimate of caffeine/day for each woman which was classified into tertiles based on the distribution at the EDO/C+2 day assessment (Low = 0-47mg/day, Medium = 48-227, High ≥228). Weighted kappa statistics (Kw) were used to determine the agreement between each retrospective assessment compared to the EDO/C+2 day. There was substantial agreement at EDO/C+18 days (Kw = 0.61, 95% CI: 0.39, 0.84) and EDO/C+6 weeks (Kw = 0.66, 95% CI: 0.43, 0.88). There was moderate agreement at EDO/C+38 weeks (Kw = 0.57, 95% CI: 0.35, 0.78). For each retrospective survey, 86%-95% of caffeine measurements were within one standard deviation of the mean of caffeine measured at EDO/C+2 (156.2 mg/day ± 195.91). These results suggest that retrospectively assessed exposures should be interpreted with caution and may only moderately agree with prospectively measured data.

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HUME, MILL, HILL, AND THE SUI GENERIS EPIDEMIOLOGIC APPROACH TO CAUSAL INFERENCE.

*Alfredo Morabia (Queens College CUNY, New York NY 10024)

The epidemiological approach to causal inference consists of reviewing sets of criteria, or viewpoints, to evaluate the causal nature of an association. The question of whether it has its origin in the thinking of English philosophers of the 18th (David Hume,[1711-1776]) and 19th centuries (John Stuart Mill [1806-1873]) has never been explicitly explored. I review here the process of causal inference based on Hume's "rules," Mill's "canons," and Hill's "viewpoints." Differences are profound. Hume does not emphasize the need for contrastive evidence, which is central to Hill's viewpoints, and Mill's canons of comparison are incompatible with observational epidemiologic study designs. Thus, neither Hume nor Mill can be considered as a precursor of Hill's viewpoints. The epidemiological approach to causal inference appears to be novel, sui generis, and still waiting for to be embedded in a philosophical explanation.

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CLINICAL TRIALS IN PEDIATRIC ONCOLOGY: THE NATIONAL CANCER INSTITUTE LEUKEMIA RESEARCH PROGRAM, 1948-1962. *Robin Rohrer (Seton Hill University, Greensburg PA 15601)

Today the survival rates of children diagnosed with acute lymphoblastic leukemia or "childhood leukemia" exceeds 90% for those diagnosed with standard risk disease. It is well recognized that the development of curative therapies for children with ALL is a major milestone in the history of medicine and epidemiological research. This work uses the archival material of the National Cancer Institute and the oral histories of the National Institutes of Health Office of History to examine the development of the first nine randomized trials in pediatric leukemias and how and why the trial questions were determined with initial results. In particular the study explores the research process behind the decision to test single modalities and combination chemotherapies.

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TRENDS AND SOCIOECONOMIC AND RACIAL/ETHNIC DISPARITIES IN ZOSTER VACCINATION IN A US MANAGED CARE ORGANIZATION. *Rulin Hechter, Ning Smith, Sara Tartof, Hung Fu Tseng (Kaiser Permanente Southern California, Pasadena CA 91101)

Objectives: Zoster vaccine is recommended for prevention of herpes zoster among adults aged 60 years and older. We examined the association between race/ethnicity, factors related to socioeconomic status (SES) and zoster vaccination rates during 2007-2011 in eligible adults at Kaiser Permanente Southern California, a managed care organization in the US. Methods: We calculated annual zoster vaccination rate among enrollees ≥60 years who had no contraindications such as HIV/AIDS, leukemia, lymphomas, or other malignant neoplasms. Multivariable logistic regression was performed to examine correlates for zoster vaccine uptake among an open cohort of 819,466 individuals with at least 6 month membership after they turned 60 years old during the study period. Results: The zoster vaccination rates increased annually in all gender and race/ethnicity subgroups, from 7.1% in 2007 to 21.7% in 2011 (P-trend < 0.0001). The overall uptake was higher among females and non-Hispanic Whites. After adjustment for age, duration of membership at baseline, and health care utilization, living in a neighborhood with higher levels of education attainment and income was associated with higher odds of zoster vaccination (>75% vs. < 50% adults with some college education: OR = 1.75, 95% CI = 1.71-1.79; annual household income ≥ $100,000 vs. < $25,000: OR = 1.22, 95% CI = 1.16-1.29). African Americans and Hispanics had significantly lower odds of vaccination than Whites (African Americans: OR = 0.57, 95% CI = 0.56-0.58; Hispanics: OR = 0.59, 95% CI = 0.58-0.60). Conclusion: Although the observed vaccination rate is higher in this population compared to the general US population, the zoster vaccine coverage remained low among eligible adults in the five years following the introduction of routine zoster vaccination. Socioeconomic and racial/ethnic disparities in zoster vaccination rates were observed in this insured population with relatively equal access to care.

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HAS MASSACHUSETTS HEALTH CARE REFORM WORKED FOR THE WORKING POOR? *Liane Tinsley, Susan Hall, John McKinlay (New England Research Institutes, Inc., Watertown MA 02472)

MA health care reform, introduced in 2006, serves as a model for federal reform. The Boston Area Community Health Survey collected data before (2002-2005; T1) and after (2006-2010; T2) introduction of the MA health insurance mandate, providing a unique opportunity to study reform effects. We sought to examine reform's effect on the working poor (WP) population of Boston, MA considering both health insurance coverage and access to care. We stratified T2 into a pre- and during-mandate and post-mandate period. Data on household income, health insurance coverage, and health care provider (HCP) visits was obtained via in-person interviews. Persons 65y at T2 were excluded, as were those no longer residing in MA (resulting N = 3,052). WP were defined as those 'currently working for pay' with household income <200% of the federal poverty threshold (FPT); non-working poor (NWP) as those reporting any work status other than "working for pay" with household income <200% of the FPT; and not poor (NP) as those reporting annual household income ≥200% of FPT. 18.5% (T1) and 17.7% (T2) of participants met the definition of WP. At T1, 26.5% of WP were uninsured, compared to 15.7% of NWP and 8.4% of NP. Among WP interviewed pre- and during-mandate at T2, 15.5% reported no health insurance compared to 10.0% interviewed post-mandate; corresponding proportions were 4.4% and 5.0%, and 9.0% and 0.9% among NWP and NP, respectively. The proportion of those with at least one HCP visit in past six months among all three groups increased following reform implementation, but was consistently lowest among WP. Our study found that both the WP and others in MA benefitted from the implementation of state health care reform, but a persistent coverage disparity suggests that its reach was not universal.

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NOCTURIA, PRESCRIPTION MEDICATION USE AND HEALTH CARE UTILIZATION: RESULTS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY. *Varant Kupelian, Susan Hall, Tove Holm-Larsen, Jens Peter Norgaard, Raymond Rosen (New England Research Institutes, Inc., Watertown MA 02742)

Waking to void ≥2 times/night is associated with increased morbidity and mortality. Using data from the National Health and Nutrition Examination Survey (NHANES), a national probability survey of the U.S. population, the objective of this study is to investigate prevalence and patterns of prescription medication use among men and women with nocturia. Nocturia was defined as 2 or more voiding episodes per night over the past month. Prescription medication use over the past month was collected from the medication label and coded using Cerner Multum's Lexicon. Analyses were conducted on 15,901 participants from NHANES III and 9,531 participants from NHANES 2005-2008. Logistic regression was used to assess the association of medication use and nocturia and adjust for potential confounders including age, race/ethnicity, body mass index, and comorbid conditions. Prevalence of both nocturia and prescription medication use increased with age in men and women. Increased use of multiple prescription medications was significantly higher among those with nocturia compared to those without nocturia, and was consistent by both gender and NHANES cycle. Odds ratios (OR) for ≥3 medications use ranged from 1.78 to 2.23 after adjusting for potential confounders. Multivariable analyses show robust association of nocturia with use of analgesics (adjusted OR and 95% confidence intervals of 1.71 (1.22, 2.49) for men and 1.32 (1.05, 1.67) for women) and calcium channel blockers (adjusted ORs of 1.74 (1.22, 2.49) for men and 1.63 (1.22, 2.18) for women) for both genders, and with antidepressants among women (adjusted OR = 1.33 (1.05, 1.67)). A significant increase in the number of health care visits was also observed among men and women with nocturia. The results of this study show a consistent association between commonly used prescription medications and number of nightly voids among both men and women after controlling for potential confounders and comorbid conditions.

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NON-STEROIDAL ANTI-INFLAMMATORY MEDICATION USE AND DEVELOPMENT OF LOWER URINARY TRACT SYMPTOMS IN MEN AND WOMEN. LONGITUDINAL RESULTS FROM THE BOSTON AREA COMMUNITY HEALTH (BACH) SURVEY.

*Varant Kupelian, Susan Hall, Andre Araujo, John McKinlay (New England Research Institutes, Inc., Watertown MA 02472)

Increasing evidence of a role of inflammation in the etiology of lower urinary tract symptoms (LUTS) suggests a possible role of non-steroidal anti-inflammatory drugs (NSAIDS) in the prevention of development and progression of LUTS. The present study investigates the association between use of prescription and over-the-counter NSAIDS and development of LUTS in both men and women. BACH is a prospective study of 4,144 participants (1,610 men and 2,534 women) with baseline assessment conducted in 2002-2005 and follow-up in 2006-2010. LUTS was defined as a score of ≥8 on the American Urological Association Symptom Index (AUA-SI) scale. A change of ≥3 points on the AUA-SI was considered clinically relevant. Logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (95% CI) of the NSAIDS and LUTS association and to adjust for comorbid conditions and sociodemographic and lifestyle factors. NSAIDS use at baseline was associated with increased likelihood of improved symptoms (decrease in AUA-SI ≥3 points between baseline and follow-up) among women (adjusted OR = 1.65, 95% CI: 1.05, 2.58) but not among men (adjusted OR = 0.94, 95% CI: 0.61, 1.46). Analyses conducted among participants without LUTS at baseline (AUA-SI<8) show a protective effect of NSAID use on development of LUTS (AUA-SI≥8) at follow-up in both men (adjusted OR = 0.54, 95% CI: 0.32, 0.91) and women (adjusted OR = 0.55, 95% CI: 0.31, 0.96). These results provide further evidence of a role of inflammation in the etiology of LUTS and the possibility that NSAIDS may inhibit development of LUTS. A consistent protective effect of NSAIDS in both men and women suggests that investigation of pathways outside of prostate inflammation may be indicated.

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FACTORS INFLUENCING PHYSICIAN ANTIMICROBIAL PRESCRIBING AT OUTPATIENT FACILITIES ASSOCIATED WITH BOSTON MEDICAL CENTER.

*Jake Morgan, Tamar Barlam, Mari-Lynn Drainoni, Cindy Christiansen, Lee Wetzler (Boston University School of Public Health, Boston MA 02118)

Despite clear clinical guidelines and strong evidence that antimicrobials are not indicated for most upper respiratory infections, prescription for the common cold, acute bronchitis, and others account for up to 40% of all antibiotics given in ambulatory care, and no published study has comprehensively evaluated appropriate prescribing through the combined effect of both physician and patient factors. To address this gap in knowledge, we developed a conceptual model to predict appropriate antibiotic prescription using both provider and patient factors, empirically validating the model with three years of retrospective data on physician characteristics and outpatient visits for upper respiratory tract infections at Boston Medical Center. These visit-specific data allow us to assess associations between practice, physician, and patient factors, examining how they are related to inappropriate antimicrobial prescribing. Bivariate analyses test associations between empirical factors and prescribing outcomes and multivariable logistic regressions quantify the predictive factor effects. The results reveal previously unreported findings, including substantial differences within clinical practices and among specific comorbidities ever after controlling for multiple covariates and individual physician effects: being a family medicine practitioner significantly predicted over-prescribing of antibiotics with an odds ratio of 1.98 (95% confidence interval 1.4 - 2.9) compared to a primary-care practice group while a patient with congestive heart failure was more likely to be under-prescribed with an odds ratio of 1.70 (95% confidence interval 1.1-2.7). The results inform future intervention to increase appropriate antibiotic prescribing as well as suggesting further investigation into clinical guidelines on prescribing in the presence of serious comorbidities.

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PROVIDER QUALITY REPORTING AND INDIVIDUAL RECEIPT OF HEALTH CARE SERVICES: EVIDENCE FROM THE SURVEY OF THE HEALTH OF WISCONSIN.

*Kristen Malecki, Lauren Wisk, Matthew Gigot, Paul Peppard, Matthew Walsh, F Javier Nieto (Survey of the Health of Wisconsin, Department of Population Health Sciences, University of Wisconsin, Madison, Middleton WI 53562)

We sought to look at the impact of system level quality reporting on patient outcomes for the Wisconsin population and for specific subsets of the population that would be impacted by certain specific health care system quality reporting initiatives and priorities. Data are from the 2008-2011 Survey of the Health of Wisconsin (SHOW) and Wisconsin Collaborative for Healthcare Quality (WCHQ). Our sample includes 2,183 adults who were matched to their usual provider. WCHQ provider performance on four preventive care and one chronic care quality reporting metrics were used to determine WCHQ provider rankings. Provider type and rankings were used to predict receipt of 9 preventive health services among those who were eligible based on USPSTF guidelines, adjusting for patient gender, age, educational attainment and health insurance status. 46.1% of SHOW participants had a WCHQ provider, 42.5% had a non-WCHQ provider, and 11.5% did not have a usual provider. Multivariable analyses revealed that individuals without any usual provider were significantly less likely to have received all 9 preventive health services compared to individuals with a regular provider. Higher provider performance increased individual receipt of biennial pap smears, biennial blood pressure check, biennial cholesterol checks, biennial general health checkup, and annual influenza vaccination. Overall, a composite quality metric better predicted receipt of services than disease-specific metrics. Provider quality reporting appears to correspond to the receipt of some, but not all, priority preventive services on the individual level. Interestingly, the composite metric better correlated with receipt of services than disease-specific metrics, suggesting that those wishing to utilize quality reporting tools may want to carefully consider how to operationalize these metrics.

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DISPARITIES IN RECEIPT OF NEEDED DENTAL CARE AND ORAL HEALTH: EVIDENCE FROM THE SURVEY OF THE HEALTH OF WISCONSIN.

*Kristen Malecki, Lauren Wisk, Lynne Morgan, F Javier Nieto (Survey of the Health of Wisconsin, Department of Population Health Sciences, University of Wisconsin, Madison WI 53562)

Oral health is an essential and integral component of overall health. Oral health surveillance data on adults in Wisconsin, as in most states, has been mostly limited to self-reported survey data. Therefore, we sought to utilize unique data, including an oral exam and survey, to understand oral health in the state, to identify who is at greatest risk of having poor oral health and what predicts someone having poor oral health. Data are from the Survey of the Health of Wisconsin (SHOW) Oral Health Screening project, conducted in partnership with the Wisconsin Department of Health Services. Our sample included 1,453 adult Wisconsin residents who completed an oral exam and SHOW questionnaires. Over 15% of Wisconsin residents who participated had untreated cavities. 20% of participants didn't get the dental care they needed; and nearly 70% of those participants said it was because of costs. Individuals who reported unmet need for dental care for any reason were four times more likely to have untreated cavities, controlling for sociodemographics and oral health behaviors. Additionally, individuals with unmet dental need were also 3.70 times more likely to have experienced regular painful aching in their mouths during the past year and 3.76 times more likely to need urgent treatment for their teeth, controlling for covariates. Additional disparities in oral health existed by socioeconomic status (education and income), health insurance status, and oral health behaviors. Even when accounting for oral health behaviors, such as brushing and flossing, the strongest predictor of poor oral health was experiencing unmet dental need in the past year.

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ALTERNATIVE HEALTH PRACTICES DURING THE PERINATAL PERIOD: WHAT CAN CURRENT DATA TELL US? *Pamela Jo Johnson, Katy Backes Kozhimannil, Neha Ghildayal (Medica Research Institute, Minnetonka MN 55305)

Use of alternative health practices, including complementary and alternative medicine (CAM), in the US is prevalent, and women of childbearing age are the most frequent users of CAM. Nearly four million women give birth in the US every year; however, little is known about the extent to which CAM is used by women during pregnancy and childbirth. Limited evidence suggests growth in CAM use as well as alternative approaches to managing perinatal symptoms and conditions, including nausea, sleep problems, and pain during labor. To date, there has been no comprehensive examination of the alternative health practices women choose or the CAM therapies being used by women during pregnancy and childbirth. Our objective was to use existing data to document current knowledge on alternative health practice use, including CAM, during the perinatal period. We assessed the extent to which publicly available survey data could be used for perinatal CAM research. Data sources examined include: National Health Interview Survey (NHIS), National Ambulatory Medical Care Survey (NAMCS), Medical Expenditure Panel Survey (MEPS), and Listening to Mothers Survey (LTM). We highlight strengths and limitations of existing national surveys for examining CAM use among women of childbearing age and specifically during pregnancy and childbirth. Cross-survey comparisons are made for prevalence, types, and reasons for CAM use with respect to availability of public use data, sample size, and variable detail. We also summarize available measures of conventional health services and health outcomes for each survey. Emphasis is on data source tradeoffs between availability of CAM measures, ability to examine integration of conventional medicine and alternative health practices, and potential for perinatal outcomes research. We offer recommendations for alternative health services data collection to enhance understanding of CAM use during pregnancy and childbirth.

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GUIDELINE APPROPRIATE RECEIPT OF THE INFLUENZA VACCINE AMONG PREGNANT WOMEN IN THE US. *Lauren Wisk, Whitney Witt (Department of Population Health Sciences, University of Wisconsin, Madison WI 53726)

Experts recommend that all pregnant women get a flu shot as the vaccine has been shown to prevent influenza and flu-related hospitalizations in women and their infants up to 6 months of age; however the nasal spray flu vaccine is not approved for pregnant women. We sought to determine the predictor of receipt of flu shot and spray among a nationally representative, population-based sample of pregnant women. We examined data on 4,180 women who were currently or recently pregnant from the 2005-2010 National Health Interview Survey. Receipt of flu shot or spray was examined during a 12 month window. Disparities in receipt of the vaccine among pregnant women were also compared against disparities in receipt of the vaccine among US mothers (N = 28,324) to determine if certain disparities were specific to pregnant women. Overall, 24.8% of pregnant women received the flu shot, with rates substantially increasing over time. Although pregnant women's receipt of flu spray was generally low before the H1N1 outbreak (0.3%), it jumped to 2.7% during the outbreak. Multivariate logistic regression revealed that black (non-Hispanic) women had lower odd of flu shot receipt during pregnancy, as did women with lapses in insurance coverage. There were additional disparities in the receipt of the flu shot by socioeconomic status, usual source of care, and health status. Racial and socioeconomic disparities were more pronounced among pregnant women than among US mothers. Publicly insured US mothers were less likely to receive the shot than privately insured mothers, while there was no such difference among pregnant women. There were regional disparities for US mothers that were not observed for pregnant women. Despite recommendations, influenza shot levels among pregnant women are generally low, pregnant women are receiving the flu spray against clinical guidelines, and there are distinct disparities in vaccination between pregnant women and US mothers.

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WITHDRAWN

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WHAT DOES THE MASSACHUSETTS EXPERIENCE TELL US ABOUT THE POTENTIAL IMPACT OF THE AFFORDABLE CARE ACT ON THE USE OF CLINICAL PREVENTIVE SERVICES? *Catherine Okoro, Satvinder Dhingra, Ralph Coates, Matthew Zack, Eduardo Simoes (Centers for Disease Control and Prevention, Atlanta GA 30333)

Background: Expansion of health insurance coverage for clinical preventive services provides an opportunity for improvements in the health of adults. There is limited research on how much expansion of health insurance coverage may affect clinical preventive service use. Objective: To examine potential effects of the 2006 health reform in Massachusetts on clinical preventive service use. Methods: We used data from the Behavioral Risk Factor Surveillance System to examine change in healthcare access and use of clinical preventive services among working-aged adults pre-reform (2002-2005) and post-reform (2007-2010) in Massachusetts compared with change in other New England states. Results: In Massachusetts, the proportions of adults who had health insurance coverage, a healthcare provider, no cost barrier to healthcare, an annual routine checkup, and a colorectal cancer screening increased significantly more than those in the other New England states. Massachusetts did not show the significant decline in cervical cancer screening observed in the other New England states. Cholesterol screening, adult influenza immunizations, and mammography screening did not improve more in Massachusetts than in other New England states. Conclusions: The Affordable Care Act may increase healthcare access and improve use of clinical preventive services. However, the effects of the Affordable Care Act on clinical preventive service use may vary by the type of service and by state.

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POLICY IMPACT ON EMPLOYMENT OF DENTAL HYGIENISTS IN NURSING HOMES IN JAPAN. *Kanade Ito, Toru Tsuboya, Jun Aida, Ken Osaka (Tohoku University, Department of International and Community Oral Health, Sendai Japan)

A lot of studies have showed that professional oral care can prevent aspiration pneumonia of residents in nursing homes. Japan's government has started a policy giving subsidies to nursing home that employ dental hygienist (DH) since 2009. There were no previous studies on health service managers' recognition of the policy, placement of DHs in nursing homes, and what factors were associated with the placement. The aim of this study was to investigate these questions. A survey questionnaire was sent to all nursing homes in Japan during Feb 2012, which contains information as follows; employment of DHs, recognitions of the policy that giving subsidies nursing homes for placement of DHs, having external evaluation of nursing homes, accepting internship, performing end-of-life care, and number of the employees (<51, 51-71, 71<). Analyzing 1,280 data from 1,484 responding (responding rate: 23.5%), we found 97.3% of nursing homes recognized the policy. The prevalence of DHs was only 9.6%. The prevalence of DHs tended to be higher in nursing homes with having external evaluations (yes: 10.4%, no: 9.3%) and accepting internship (9.7%, 9.4%) although statistical significant differences were not found. Number of employees and performing end-of-life care were significantly associated with hiring DHs; the prevalence of DHs at small, middle and large nursing homes were 5.1%, 10.8% and 13.2%, respectively (p for trend < 0.001), and performing end-of-life care in nursing homes were 13.2% for yes and 5.6% for no ($p < 0.001$). This study showed that only 10% of nursing homes employed DHs although 97% of nursing homes recognized the policy. The policy was not necessarily support for placement of DHs in nursing homes. It is possible that larger-sized nursing homes tend to employ more professional staff, such as registered nurses and DHs, and can give residents more comprehensive care, including end-of-life care.

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PATIENT EVALUATION ABOUT HEALTHCARE QUALITY IN HEALTH CENTER. *Cláudia Chaves, Paula Nelas, Emília Coutinho, João Duarte, Nélio Veiga (CI&DETS, Polytechnic Institute of Viseu - Portugal)

Background: Patient evaluation of practice is of the upmost importance when speaking of healthcare quality, being their opinion pivotal in healthcare quality assessment. Objectives: To assess the level of satisfaction of patients at Health Center of Portugal, using EUROPEP items and scales; to describe the level of satisfaction regarding nursing items; to determine at what level socio-demographic variables may influence patient evaluation of healthcare; to determine the influence of state of health variables over patient evaluation of healthcare. Methods: 1172 patients at a Health Center (HC) in Portugal were invited to complete a questionnaire based on the EUROPEP instrument. Factor analysis was based on quantitative, transversal descriptive- correlational and exploratory statistics (average age = 46, 25 years; mean desviation = 17, 77 years). Results: 61.7% were female, 44.9% of users found in the literacy level "low"; 33.9% of users ranked their health as "good", 20.6% reported having hypertension; the females patients had a higher number of consultations with their General Practitioner (M = 2.95 visits/year);Regarding the items Health Center facilities and healthcare, there is significant correlation between patients' sex and healthcare evaluation; Regarding age and patient satisfaction we verify a significant effect on assessment of every item except Health Center facilities and healthcare; The effect of schooling level on patient satisfaction is relevant on every item except on Healthcare management, HC facilities and healthcare; Regarding Overall State of Health and patient satisfaction, we observe a significant effect of the first on the items Healthcare management, Post-experience assessment, Nursing Help Relation, Interpersonal and Instrumental assessment, HC facilities and Healthcare and Practitioners. Conclusions: The perception of users about the care cannot be forgotten because it contributes decisively to the improvement of the same.

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PREVALENCE OF FISSURE SEALANTS IN A PORTUGUESE SAMPLE OF ADOLESCENTS. *Nelio Veiga, Carlos Pereira, Marco Baptista, Claudia Chaves, Paula Nelas, Odete Amaral, Manuela Ferreira, Paula Ferreira, Ilidio Correia, Ines Coelho (Health Science Department UCP; CI&DETS-Polytechnic Institute of Viseu; Beira Interior University; IPATIMUP FMUP; CPEFPRC-FCTUC; FHU Grao Vasco, Portugal)

Background: The use of fissure sealants is an effective intervention for the primary prevention of pit and fissure caries in children and adolescents. The objective of this study was to determine the prevalence of fissure sealants in a portuguese sample of adolescents. Participants and Methods: A sample of 293 adolescents aged 12 to 18 years old, attending a public school in Satao, Portugal, was enrolled in this cross-sectional study. A self-administered questionnaire with questions about oral health behaviours, knowledge and socio-economic status was answered by the adolescents in the classroom. Clinical examination of oral health status and assessment of fissure sealants was accomplished by a trained and calibrated research team. The presence of fissure sealants in each tooth was assessed as total or partial. Prevalence was expressed in proportions and compared by the chi-square test. Crude odds ratio (OR) with 95% confidence intervals (CI) were used to measure the strength of association between the presence of fissure sealants and the independent variables. : Results: We verified that 26.3% (95% CI = 25.0-34.0) of adolescents refer knowing the definition of a fissure sealant, while only 5.9% (95% CI = 4.3-7.0) refer having fissure sealants applied on their teeth. The prevalence of fissure sealants was 52.7% (95% CI= 35.0-46.0), higher among the female gender (59.6% vs 46.2%, $p = 0.03$). The presence of fissure sealants was associated with a lower prevalence of dental caries (dental caries, OR = 0.32, 95% CI = 0.18-0.59) and residence area (rural, OR = 2.24, 95% CI = 1.25-4.02). Among the adolescents with at least one tooth with fissure sealants, 21.7% (95% CI = 13.9-30.0) presented total fissure sealants in sealed teeth, while 78.3% (95% CI = 70.1-86.1) presented one or more teeth with partial fissure sealant. Conclusions: We found a low prevalence of fissure sealants and a high prevalence of partial and infiltrated sealants among adolescents. A low prevalence of adolescents know the definition and indications of a fissure sealant. It is necessary the establishment of a more targeted preventive program with better and more effective oral health education.

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A CASE-CONTROL SUDY OF CLASS- AND SSSIGNMENT-SCHEDULES AS FACTORS AFFECTING UNIVERSITY STUDENT BLOOD DONATION IN GRENADA, WEST INDIES. *Sarah N Hewitt, Locksley L. McV Messam (St. Georges University, School of Medicine, St. Georges, Grenada, West Indies)

Blood transfusions burden the Grenadian healthcare system, as blood donor prevalence is low (0.5%). This is reflective of insufficient promotion of once-a-month blood drives organized by the Grenada Blood Bank and St. George's University (SGU) American Medical Students Association on SGU's campus. An incidence density case-control study was undertaken to identify class- and assignment-schedule related factors acting close to the day of a campus blood drive that affect student donation. Data were collected by interviewer-administered questionnaire on the three blood drive days in February, March, and April 2010 and only during blood collection periods (9:00 am – 3:00 pm). Cases (69) were students donating blood at any of the blood drives and controls (442) were students who did not. Proportionately less cases (16%) were Caribbean students than controls (43%) and vice versa for North American students (73% vs. 47%). Slightly more cases (64%) than controls (60%) were female. Data were analyzed using logistic regression with adjusted odds ratios approximating incidence rate ratios (IRR). Donation rates for students who did not have assignments due the day before (IRR = 1.1; 95% CI: 0.6-1.9) the blood drive were similar to those who did. However, rates for those not having assignments due the day of (IRR = 1.7; 95% CI: 0.9-3.2) or the day after (IRR = 1.5; 95% CI: 0.9-2.8) the blood drive were higher than for those who did. Donation rates for students with no classes from 9:00 am to 12:00 pm (IRR = 1.5; 95% CI: 0.8-2.9) or 12:00 to 3:00 pm (IRR = 1.9; 95% CI: 1.2-3.2) on the day of the blood drive were both higher than for those students who had classes during those times. When possible, promotion should target student groups having no assignments due the day of or the day after the blood drive, as well as, those without classes in the morning or afternoon of the day of the blood drive.

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COMORBIDITIES AND MEDICATION USE IN LUPUS NEPHRITIS PATIENTS - A COMPARISON OF RESULT ACROSS CASE IDENTIFICATION ALGORITHMS. *Kathleen McCarty, Douglas Clark, Wei-Shi Yeh (Biogen Idec, Cambridge MA 02142)

Objective: Lupus nephritis (LN) is a severe complication of systemic lupus erythematosus (SLE). While LN has no designated ICD-9 code, various approaches have been used to identify patients in administrative data. The objective was to compare comorbidities and medication use in LN patients using different algorithms in a single data source. Methods: This study used the Impact Database, a commercial insurance claims database. SLE patients were identified using ICD-9 code 710.0 from ≥2 outpatient or 1 inpatient claims from 01/2004 to 06/2011. SLE patients with LN were further identified under four different algorithms: (A) ≥1 renal diagnosis (B) ≥2 renal diagnoses (C) ≥3 renal diagnoses, and (D) ≥3 renal diagnoses plus ≥3 nephrologist visits. Comorbid conditions and prescriptions were examined for 12 months post index date of first renal diagnosis. Results: 93,957 patients were diagnosed with SLE. Among them, 24,357, 11,054, 8,895, and 6,307 cases had LN using algorithms A-D. LN cases identified by algorithms A-D had similar mean age (48.3, 46.7, 46.3, and 45.7 years) and gender distribution (85.2, 83.1, 82.7, and 81.8% females). LN patients from different algorithms also had similar distribution of comorbid conditions (urinary tract system, hypertension, anemia, heart disease, respiratory outcomes and others)and medication use (corticoids and hormones, renin angiotensin antagonists, anti-infective drugs, analgesic narcotics, diuretics and antimalarial drugs). Conclusion: Our results support that when studying patient profiles including comorbidities and medication use, the results do not differ significantly based on the number of renal diagnoses codes. There is a difference in outcomes when requiring number of patients plus specialty subtype; however, in the case where specialty information is either unavailable or unreliable, using algorithms A-C proved equally reliable in an administrative claims database.

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EFFECTS OF CHILDHOOD AND ADOLESCENT BLOOD LEAD LEVELS ON BEHAVIORAL OUTCOMES IN MONTEVIDEO, URUGUAY. Fiona Fordyce, Clarence K Zhang, Maria Jose Moll, Antonio Pascale, Silvana Couto, Adriana Sosa, Dario Pose, Laura Viola, Hongyu Zhao, Amalia Laborde, *Kathleen M McCarty (Yale University School of Public Health, New Haven CT 06520)

Introduction: Lead is a neurotoxin with childhood being a key period of exposure. Childhood lead exposure can interfere with neural development and subsequent behavioral problems. Objectives: Investigate the relationship between blood lead level (BLL's) (2001 and 2011) and behavioral outcomes in a group of Uruguayan adolescents. Methods: 91 adolescents (mean age 15.8 years), identified as having elevated BLL's in 2001 (mean = 14.4 μg/dL, SD = 6.2) were tested for current BLL's (mean = 5.4 μg/dL, SD = 2.6) using atomic absorption spectrometry. Interviewers administered the Child Behavior Checklist, a standardized assessment of behavioral problems. Linear regression was used to assess the relationship between blood lead level and behavioral outcomes. Results: 2001 BLL's were found to be significantly associated with total problem behavioral score (β = 0.51, 95% CI = 0.01-1.01), as well as somatic (β = 0.65, 95% CI = 0.19-1.11), aggressive (β = 0.37, 95% CI = 0.03-0.71), internalizing (β = 0.57, 95% CI = 0.06-1.07), and externalizing (β = 0.48, 95% CI = 0.03-0.93) problem subscales when controlling for 2011 BLL's and age. Current (2011) BLL's were not found to be significantly associated with behavioral outcomes. Conclusions: This study suggests increased childhood exposure to lead is associated with subsequent negative behavioral outcomes. Despite reduction in blood lead levels a decade later, an elevated risk of adverse behavior remains in adolescents with elevated childhood blood lead levels.

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ASSOCIATION BETWEEN HYPERTENSION AND DIETARY PATTERNS IN AN URBAN COMMUNITY OF NEPAL. *Archana Shrestha, Annette Fitzpatrick, Rajendra Koju, Shiva Gautam, Kenneth J Mukamal, Biraj Man Karmacharya, Chandra Yogal, Akina Shrestha (University of Washington, Seattle WA 98195)

Background: The association between food intake and hypertension may vary across cultures. We investigated the associations between dietary patterns and hypertension in an urban residents of Nepal. Methods: It is a cross sectional study of 200 Nepalese adults (44% males) 30 years of age or older residing in two regions of central Nepal (Kathmandu and Dhulikhel) in 2009. We selected participants through a cluster random sampling method using voter registration lists. Hypertension was defined as a systolic blood pressure of 140mmHg or higher, diastolic blood pressure of 90mmHg or higher, or being on antihypertensive medication. We collected dietary data via in-person interview using a food frequency questionnaire. Principal component analysis (PCA) was applied to extract food patterns from 22 food groups. Multivariate logistic regression evaluated the associations between the extracted dietary factors and hypertension. Result: Seven components were derived from the PCA explaining 59% of the total variation in food intake: 1) fruit, dairy products, nuts, caffeine, processed food, fats, and sweets; 2) meat and fish; 3) roots, tubers, pulses, and bread/noodles; 4) cereal and vegetables; 5) deep fried foods, 6) green leafy vegetables; and 7) milk. Component 1 explained 22% of the total variance. Other six components explained from 7.9% (component 2) to 4.6% (component 7) of the total variance. Component 5 representing deep fried foods were positively associated with hypertension. The association was significant in univariate analysis [Odds ratio (OR):1.38, 95% confidence interval (CI): 1.03-1.85, p-value: 0.03] and was numerically stronger and marginally significant after adjusting for demographic and cardiovascular risk factors (OR: 1.81, 95% CI: 0.99-3.30, p-value: 0.05). Conclusion: The patterns derived in our work in Nepalese adults suggest that deep fried foods are the most important dietary component related to the prevalence of hypertension.

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WEIGHT STATUS, MORBIDITY, AND INCIDENT DISABILITY AMONG MIDDLE AGED FILIPINO WOMEN. *Benjamin Capistrant, Linda Adair (University of North Carolina - Chapel Hill, Chapel Hill NC 27514)

Background: Low and middle income countries (LMICs) face rapidly aging populations, morbidity expansion, and increasing prevalence of overweight/obesity. Although obesity has been associated with disability incidence in many studies in higher income countries, it is not clear whether these associations hold in LMICs. Moreover, many of these studies to date have used statistical adjustment for time-varying confounding, which may result in biased estimates. Methods: We followed middle-aged women (baseline age: 42.4 ± 5.9) from the Cebu Longitudinal Health and Nutrition Survey cohort who were disability-free in 1998 (mobility disability, n = 1,494; activities of daily living, ADL, n = 1,829) over three follow-up waves (2002, 2005, 2007). We used marginal structural models (MSMs) to estimate the direct effect of high waist circumference (WC; >80cm v. ≤80 cm) on incident self-reported disability (any mobility or ADL limitation, respectively). MSMs were estimated with stabilized inverse probability weights (IPW) to account for time-varying confounding (socioeconomic status and physical activity) and mediation (morbidity: sum of self-reported arthritis, high blood pressure, heart disease, diabetes, and cancer). We fit a weighted logistic model, adjusted for time-invariant demographic factors (age, menopause status, education); models accounted for repeated observations and time. Results: Over follow-up, there were 566 and 196 incident events of mobility and ADL disability, respectively. In final IPW models that account for time-varying confounding and mediation, high WC was associated with elevated odds of mobility disability (odds ratio (OR) = 1.34; 95% confidence interval (CI): 1.03, 1.74) and ADL disability (OR = 1.87; 95% CI: 1.19, 2.93). Conclusions Our results found a controlled direct effect of obesity on incident disability. Addressing obesity will be important to reduce disability and chronic disease morbidity among middle and older age women in LMICs.

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RACIAL DISPARITIES IN LIFE EXPECTANCY IN BRAZIL: CAUSES AND IMPLICATIONS FOR A MULTIRACIAL FUTURE. *Alexandre Chiavegatto Filho, Hiram Beltran-Sanchez, Ichiro Kawachi (School of Public Health, University of Sao Paulo, Sao Paulo SP Brazil)

Objectives: To use recently published results from Brazil's 2010 Census to calculate life expectancy at birth for whites, blacks and mixed-races and compare it to US data. Methods: We used official death records from the Ministry of Health and population data from the 2010 Census, totaling 190,755,799 residents and 1,136,947 deaths. Decomposition of life expectancy by cause of death was calculated by applying the Arriaga methodology. Sensitivity analyses were performed for underreporting, missing data and the numerator-denominator bias. Results: We found an initial pattern of life expectancy disparities that was contrary to expectations, based on racial socioeconomic inequalities. Female life expectancy was highest for mixed races (78.80), followed by whites (77.54) then blacks (76.32). For males, life expectancy was highest for whites (71.10) followed closely by mixed races (71.08), and lower for blacks (70.11). When comparing the results from the decomposition according to cause of death with US data, we found no clear trend that could explain the difference between the two countries. After adjusting for underreporting, missing data and the numerator-denominator bias, life expectancy for males and females was highest for whites in comparison with blacks/mixed races, but the gap was still smaller than for the US (4.60 years for males and 2.47 for females in Brazil, and 5.44 and 3.71 in the US). Conclusions: We found evidence that the racial gap in life expectancy is smaller in Brazil in comparison with the US, despite Brazil's higher racial socioeconomic disparities. The recent blurring of racial boundaries, a fast-growing reality for most countries, introduces new challenges for the quantification of racial inequalities. Studies on health disparities will need to better address issues of underreporting, missing data and the numerator-denominator bias.

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PREDICTORS OF LOSSES TO FOLLOW-UP (LTFU) AND A RETURN TO CARE IN AN ANTIRETROVIRAL THERAPY (ART) PROGRAMME IN ZOMBA, MALAWI. *Beth Rachlis, Monique van Lettow, Michael Escobar, Farah Ahmad, James Orbinski, Donald C Cole (University of Toronto, Toronto ON Canada)

Background: Retention in ART programmes remains a challenge in many settings. Patients who are LTFU need to be traced in order to confirm their status and encourage their return to care. However, tracing can be costly and limited resources may be used to trace individiuals who ultimately return on their own. We sought to determine the predictors of becoming LTFU as well as the predictors of a subsequent return to care. Methods: All patients who initiated ART in Dignitas International supported sites in Zomba, Malawi between January 1 2007-June 30 2010 were eligible for inclusion. LTFU was defined as being ≥56 days late for an expected visit. Generalized Estimating Equations logistic regression was used to determine the predictors of LTFU and among those classified as LTFU, the predictors of a return to care within 12 months of an expected visit. Results: In total, n = 5606 patients with n = 17797 visits were included. While some factors were consistent in predicting both LTFU risk and a return to care (time on ART and World Health Organization stage at ART initiation), the majority of variables examined demonstrated differences across models: female gender (Odds Ratio, 95% Confidence Interval: 0.79, 0.69-0.90), being married (0.79, 0.70-0.90) and a ≥10% weight gain since baseline (1.48, 1.13-1.92) were predictive only of LTFU risk while transferring in (0.40, 0.24-0.69) and being in centralized care (0.35, 0.24-0.50) were predictive only of a return to care. Discussion: Strategies to address retention should target those with an increased risk of both becoming and remaining LTFU. Patients in the earlier stages of treatment for example, should be prioritized for tracing. Our findings also suggest that some factors may play different roles in either predicting an initial risk of becoming LTFU or among those already lost, the likelihood that they return to care. Further study is needed to identify additional relevant predictive factors in other datasets.

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SOCIOECONOMIC PATTERNING OF HYPERTENSION IN GRENADA. *Eric Roberts, Leigh Quarles, Rajesh Vedanthan, Marcelle Lewis, Marilyn Hunn, Michael Farkouh, Valentin Fuster, Bernadette Boden-Albala (Mount Sinai School of Medicine, New York NY 10029)

Over 80% of cardiovascular disease deaths occur in low and middle income countries with approximately two-thirds of stoke and one-half of ischemic heart disease estimated to be due to non-optimal blood pressure. Much is known about the social epidemiology of hypertension (HT) in "Western" contexts but less is known about these associations in "non-Western" contexts. This study describes the socioeconomic patterning of HT in a population of Grenadians. The Grenada Heart Project surveyed 2827 persons between 2008 and 2010. We explored the association between education, income, occupation, nativity, residing in either the United States or Europe at one point in time, and parish of residence with definitive HT (≥140/90 mmHg) in separate logistic regression models adjusting for age and sex. The sample was 57.5% female with a mean age of 44.8 (sd = 17.1). Participants that did not complete primary school [Odds Ratio (OR) = 2.04, 95% Confidence Interval (CI) 1.37, 3.02], participants that completed primary school [OR = 1.82, 95% CI 1.29, 2.58], and participants that attended or completed secondary school [OR = 1.48, 95% CI 0.99, 2.21] had increased odds of having HT compared to those with more than a secondary education. Compared to government employees, homemakers [OR = 2.45, 95% CI 1.52, 3.95], retired persons [OR = 2.40, 95% CI 1.69, 3.42], and unemployed persons that are unable to work [OR = 2.85, 95% CI 1.59, 5.11] had increased odds of having hypertension whereas non-government employees [OR = 1.09, 95% CI 0.79, 1.50], self-employed persons [OR = 1.09, 95% CI 0.96, 1.85], and unemployed persons that are able to work [OR = 1.09, 95% CI 0.68, 1.69] did not have significantly different odds of HT. We found significant differences in the prevalence of HT by parish. Income, nativity, and history of residing in western countries was not associated with HT. We find patterning of HT by socioeconomic status in a country undergoing the epidemiologic transition.

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THE EFFECT OF A DELIVERY FEE EXEMPTION POLICY ON SOCIOECONOMIC INEQUALITIES IN HEALTH FACILITY DELIVERIES: A DIFFERENCE-IN-DIFFERENCES ANALYSIS FROM FIVE WEST AFRICAN COUNTRIES. *Britt McKinnon, Sam Harper, Jay Kaufman, Yves Bergevin (McGill University Department of Epidemiology, Biostatistics and Occupational Health, Montreal QC Canada)

User fees are prevalent in many African countries and are recognized as a major barrier to increasing utilization of reproductive health services, especially among the poor. We took advantage of a natural experiment whereby three African countries (Burkina Faso, Senegal, and Ghana) adopted policies abolishing or reducing user fees for deliveries between 2003-2007 and evaluated whether this policy change led to a reduction in socioeconomic inequality in the proportion of deliveries that occurred in a health facility. Using Demographic and Health Survey data from Burkina Faso, Cameroon, Ghana, Nigeria, and Senegal, we employed a difference-in-difference-in-differences (DDD) approach that accounts for underlying secular trends common across countries, time invariant differences among countries, and allows for differential effects of the policy according to socioeconomic position. We used an asset-based wealth quintile variable as our measure of socioeconomic position and controlled for other individual characteristics (e.g., maternal age). According to our DDD model, the delivery fee exemption policy was associated with absolute increases of 16.7 per hundred live births (95% confidence interval (CI): 12.6, 20.7) and 6.8 per hundred live births (95% CI: 3.4, 10.3) in facility deliveries among births in the poorest and richest quintiles, respectively. The richest-poorest quintile difference declined by 9.8 facility deliveries per 100 births (from a difference of 41.3 to 31.5) in the presence of the policy and the richest-poorest quintile ratio was reduced from 2.4 (95% CI: 2.3, 2.6) to 1.7 (95% CI: 1.5, 1.8). Our findings suggest that adoption of a user fee exemption policy for deliveries led to a reduction in both absolute and relative socioeconomic inequalities in health facility deliveries. Evidence from this and other user fee policy evaluations will be useful to governments weighing the potential benefits of policy changes that abolish user fees for reproductive health services.

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SLEEP PROBLEMS IN RELATION TO KIDNEY DISEASE AMONG SUB SAHARAN AFRICANS. *Bizu Gelaye, Michelle Williams, Yemane Berhane (Harvard School of Public Health, Boston MA 02115)

Objective: Sleep problems, including short sleep duration and poor sleep quality, are common though understudied conditions that may be associated with increasing risks of chronic diseases among sub Saharan Africans. We examined the association of sleep problems with kidney disease among sub Saharan African adults. Methods: The study was conducted among 1,090 adults attending an outpatient department in a major referral hospital in Addis Ababa, Ethiopia. Structured interviews were conducted to collect information about participants' demographic and behavioral characteristics. The Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep habits and quality. Kidney disease (KD) was defined by self-reported physician diagnosis. Multivariable logistic regression was used to estimate adjusted odds ratios (AORs) and 95% confidence intervals (CIs) for various sleep problems according to KD status. Results: Sleep problems were common with approximately 60% of participants grouped as having poor sleep quality. Participants with KD were more likely than those without KD to report multiple sleep problems. After adjustment for potential confounders, compared to patients without KD those with KD were more likely to have poor sleep quality (AOR = 2.22; 95% CI: 1.62-3.03), short sleep duration (AOR = 1.77; 95% CI, 1.33-2.35), long sleep latency (AOR = 1.78; 95% CI, 1.34-2.38), daytime dysfunction due to sleep problems (AOR = 1.83; 95% CI, 1.33-2.53), poor sleep efficiency (AOR = 1.59; 95% CI, 1.18-2.13), and sleep medication use (AOR = 3.09; 95% CI, 1.46-6.54) were all positively associated with KD. The relationship between KD and sleep problems was not explained by body mass index, history of diabetes or hypertension. Conclusion: Kidney disease is associated with a higher risk of sleep problems. Prospective studies are needed to confirm our findings and to more thoroughly explore the potential mechanisms for sleep problems in KD patients among sub Saharan Africans.

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THE EFFECTS OF RACE, ETHNICITY AND MOOD/ANXIETY DISORDERS ON THE CHRONIC PHYSICAL HEALTH CONDITIONS OF MEN FROM A NATIONAL SAMPLE. *Vicki Johnson-Lawrence, Derek Griffith, Daphne Watkins (University of Michigan, Ann Arbor MI 48109)

Racial/ethnic differences in health are evident among men. Previous work suggests associations between mental and physical health but few studies have examined how mood/anxiety disorders and chronic physical health conditions co-vary by age, race, and ethnicity among men. Our study examined associations between race/ethnicity and experiencing 1+ chronic physical health conditions in logistic regression models stratified by age (<45 or 45+ years) and 12 month mood/anxiety disorder status (none or any). Data were from 1277 African American, 629 Caribbean Black, and 371 non-Hispanic White male respondents from the National Survey of American Life. Mood/anxiety disorders included major depressive disorder, dysthymia, bipolar disorder, panic disorder, agoraphobia, social phobia, and generalized anxiety disorders assessed using the Composite International Diagnostic Instrument. Chronic physical health conditions included blood circulation problems, heart trouble or heart attack, hypertension, diabetes, kidney problems, stroke, cancer, asthma, chronic bronchitis, and emphysema. Findings showed Caribbean Black men <45 years without mood/anxiety disorders had lower odds of 1+ chronic physical health conditions than White men <45 years without mood/anxiety disorders (OR = 0.49, 95% CI = 0.26-0.91), and African American men <45 years with mood/anxiety disorders had greater odds of 1+ chronic physical health conditions than White men <45 years with mood/anxiety disorders (OR = 0.08, 95% CI = 0.01-0.48). Future studies should explore the underlying causes of such variations, how jointly studying mental and chronic physical health problems may help to identify mechanisms that underlie racial disparities in life expectancy among men.

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POPULATION-BASED PATTERNS OF TESTOSTERONE USE, 1976-2008. *Susan Hall, Gayatri Ranganathan, Liane Tinsley, Jennifer Lund, Varant Kupelian, Philip Kantoff, Gary Wittert, Andre Araujo (New England Research Institutes, Inc., Watertown MA 02472)

Prescription testosterone (T) has a narrow range of approved medical indications and is a controlled substance in Canada and elsewhere due to its potential for misuse and abuse. Despite sharp increases in sales volume and the advent of direct-to-consumer advertising for T in the U.S., there is little information regarding population-based patterns of androgen use in developed countries. Using data based on electronic records of dispensed prescriptions, we conducted a population-based study (1976-2008) to examine medical use of androgens, including T, among adult (18+) men in Saskatchewan, Canada: a discrete jurisdiction of universal health care. Over the 32-year study, data were missing for an 18-month period (July 1987-Dec 1988). To examine time trends, we calculated annual androgen prescription dispensing event rates per 18+ male population per year using provincial census data. There were 11,521 men who used androgens during the study period. Only injected and orally-administered formulations of androgens were listed in the provincial formulary. Overall, 11 types of androgens were used and 86,812 prescriptions were dispensed. The mean age at first use was 56.4 (median: 58). Men were dispensed 7.5 prescriptions on average (median: 2); 89.9% were prescribed by a general practitioner. The most commonly-used formulations were methyl-T (36.2% of users) followed by T-enanthate (32.5%), T-cypionate (22.3%) and T-undecanoate (20.0%). Most users (82%) did not switch among androgen types. Over the first 20 years of the study period, the annual rate of prescription dispensing events per population was relatively constant (approximately 5.0 per 1000), but began to increase from 1997-98, and thereafter remained >10.0 per 1000 from 1999-2008. Our population-based study adds to the scant epidemiologic literature on androgen utilization and suggests increasing use of androgens over time.

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COMMON PRESCRIPTION MEDICATION USE AND ERECTILE DYSFUNCTION. RESULTS FROM THE BOSTON AREA COMMUNITY HEALTH (BACH) SURVEY. Varant Kupelian, *Susan Hall, John McKinlay (New England Research Institutes, Inc., Watertown MA 02472)

Whether prescription medication use contributes to erectile dysfunction (ED) in addition the effect of the underlying illness itself (e.g. hypertension) remains controversial. The objectives of this analysis were to investigate the association of ED with commonly used medications including antihypertensive, psychoactive medications, and pain and anti-inflammatory medications. The Boston Area Community Health (BACH) Survey used a multistage stratified design to recruit a random sample of 2,301 men age 30-79. ED was assessed using the 5-item International Index of Erectile Function (IIEF-5). Prescription medication use was captured using a combination of drug inventory and self-report with a prompt by indication; medications, included in this analysis were antihypertensive agents (AHT), psychoactive medications, and pain and anti-inflammatory medications. Logistic regression was used to estimate odds ratios of the association of medication use and ED and adjust for potential confounders including age, comorbid conditions, and sociodemographic and lifestyle factors. Multivariable analyses show benzodiazepines (adjusted OR = 2.34, 95% CI: 1.03, 5.31) and tricyclic antidepressants (adjusted OR = 3.35, 95% CI:1.09, 10.27) were associated with ED, while no association was observed for SSRI/SNRIs (selective serotonin reuptake inhibitors/serotonin-norepinephrine reuptake inhibitors) and atypical antipsychotics. AHT use, whether in monotherapy or in conjunction with other AHTs, and pain or anti-inflammatory medications were not associated with ED after accounting for confounding factors. Results of the BACH study suggest adverse effects of some psychoactive medications (benzodiazepines and tricyclic antidepressants). No evidence of an association of AHT or pain and anti-inflammatory medication with ED was observed.

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ASSOCIATION OF MICROVASCULAR ENDOTHELIAL DYSFUNCTION AND ERECTILE DYSFUNCTION. *Rachael Gerber, Joseph Vita, Peter Ganz, Andre Araujo, Raymond Rosen, Varant Kupelian (New England Research Institutes, Inc., Watertown MA 02472)

Increasing evidence of a link between erectile dysfunction (ED) and cardiovascular disease (CVD) suggests a common systemic vascular etiology with endothelial dysfunction as one possible underlying biological mechanism. The objective of this study is to investigate the cross-sectional association between ED and endothelial function assessed by brachial artery reactivity. A total of 390 men were recruited from the Boston Area Community Health (BACH) Survey, a population-based study of urologic symptoms. ED, assessed using the 5-item International Index of Erectile Function (IIEF-5), was defined as an IIEF-5 score <17 (mild/moderate to severe symptoms). Brachial artery flow-mediated dilation (FMD) (%) and hyperemic blood flow velocity (cm/s), which are tests of macrovascular and microvascular endothelial function respectively, were assessed by ultrasound. Linear regression methods were used to assess the association of ED and endothelial function measure. Mean (SD) age of the study sample was 55.5 (11.2) years (range: 37, 85) and prevalence of ED was 29%. Mean (SD) FMD was lower among men with ED [6.6(3.4)] vs. without ED [7.2 (3.9)], however, this difference was statistically non-significant ($p = 0.18$). A statistically significant difference in hyperemic velocity was observed for men with ED [98.0 (26.8)] vs. without ED [105.9 (25.8), $p = 0.01$]. This difference was attenuated and non-significant ($p = 0.42$) in multivariable analyses controlling for age, BMI, smoking, CVD, hypertension, and diabetes. Significant correlations of hyperemic velocity with age ($r = -0.395$) and BMI ($r = 0.114$) were observed. Results of this study suggest impaired microvascular function among men with ED that is attributable to associated cardiovascular risk factors. These findings are consistent with the hypothesis that risk factor-induced changes in microvascular endothelial function contribute to the pathogenesis of E.D.

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TESTOSTERONE THERAPY AND CARDIOVASCULAR EVENTS AMONG MEN: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PLACEBO-CONTROLLED RANDOMIZED TRIALS. Lin Xu, Guy Freeman, Benjamin Cowling, *C Mary Schooling (The University of Hong Kong, Pokfulam Hong Kong SAR China)

Testosterone therapy is increasingly promoted. No randomized placebo-controlled trial has been implemented to assess the effect of testosterone therapy on cardiovascular events, although very high levels of androgens are thought to promote cardiovascular disease. The authors conducted a systematic review and meta-analysis of placebo-controlled randomized trials of testosterone therapy among men lasting 12+ weeks reporting cardiovascular-related events. Two reviewers independently searched PubMed through end 2012 using "("testosterone" or "androgen") and trial and ("random*")" limited to studies of men in English, supplemented by a bibliographic search and a search of the WHO trial registry; they then selected and assessed study quality independently. All differences were resolved by consensus. Two statisticians independently abstracted and analyzed data, using random or fixed effects models, as appropriate, with inverse variance weighting. Of 1882 studies identified 27 trials were eligible including 2980, mainly older, men who had 180 cardiovascular-related events. Testosterone therapy increased the risk of a cardiovascular-related event (odds ratio (OR) 1.54, 95% confidence interval (CI) 1.09 to 2.18). The effect of testosterone therapy varied with source of funding (p-value for interaction 0.03). In trials not funded by the pharmaceutical industry the risk of a cardiovascular-related event on testosterone therapy was greater (OR 2.06, 95% CI 1.34 to 3.17) than in pharmaceutical industry funded trials (OR 0.89, 95% CI 0.50 to 1.60). Overall, and particularly in trials not funded by the pharmaceutical industry, exogenous testosterone increased the risk of cardiovascular-related events, with corresponding implications for the use of testosterone therapy and for environmental exposures which raise androgens. Systematic review reference number CRD42011001815.

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ANDROGEN ACTIVITY AND ISCHEMIC HEART DISEASE AMONG MEN IN NHANES III. *C Mary Schooling (CUNY School of Public Health at Hunter College, New York NY 10035)

Observationally low serum testosterone among men is associated with cardiovascular diseases and its risk factors, but it is unclear whether raising androgens would be protective. It is possible that serum testosterone may be a marker of health status rather than a biomarker of androgen activity because anti-androgens have recently been shown to be effective in prostate cancer at castrate levels of serum testosterone. To clarify the role of androgens in cardiovascular disease the association of two different androgen biomarkers (serum testosterone and androstanediol glucuronide) with cardiovascular risk factors and death from specific cardiovascular diseases was examined in a nationally representative sample of 1498 US men from NHANES III phase 1 (1988-91) followed-up through 2006 using multivariable linear and proportion hazards regression. Serum testosterone and androstanediol glucuronide were weakly correlated (0.14). Serum testosterone was associated with healthier values of most cardiovascular disease risk factors but not with death from ischemic heart disease or stroke, adjusted for age, education, race/ethnicity, smoking and alcohol use. Similarly adjusted, androstanediol glucuronide was associated unhealthier values of some cardiovascular risk factors and death from ischemic heart disease (hazard ratio 1.17, 95% confidence interval 1.02 to 1.34 per standard deviation). Androgen biomarkers had inconsistent associations with cardiovascular disease risk factors and ischemic heart disease suggesting they represent different entities. Androstanediol glucuronide, rather than serum testosterone, had associations with cardiovascular risk and associated factors more similar to those seen in meta-analysis of randomized controlled trials of testosterone therapy, with corresponding implications for therapies or environmental exposures which raise androgens.

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MEAT INTAKE AND SEMEN QUALITY AMONG PHYSICALLY ACTIVE YOUNG MEN. *Myriam Afeiche, Paige Williams, Jaime Mendiola, Audrey Gaskins, Niels Jørgensen, Swan Shanna, Jorge Chavarro (Harvard School of Public Health, Boston MA 02115)

Introduction: In the United States, anabolic sex steroid hormones are administered to cattle and other animals for growth promotion. Scientific concern has been raised regarding the reproductive health consequences of the hormonal residues in edible tissues. High maternal beef consumption during pregnancy has been associated with lower sperm concentration among their sons 30 years later. However, it is not known whether men's meat consumption is associated with semen quality given the paucity of literature on this topic. Material & methods: The Rochester Young Men's Study ($n = 189$) was a cross-sectional study among men aged 18-22 years, conducted from 2009-2010 at the University of Rochester. Diet was assessed via food-frequency questionnaire. Linear regression was used to analyze the relation between meat intake and semen quality parameters (sperm count, concentration, progressive motility, and morphology) adjusting for age, abstinence time, race, smoking status, body mass index, recruitment period, moderate-to-intense exercise, and calorie intake. Results: Processed meat intake was inversely related to total sperm count (p-trend = 0.06) and progressive sperm motility (p-trend = 0.08). While these associations were not statistically significant, intake of unprocessed red meat was associated with significantly higher percent morphologically normal sperm. The adjusted difference in normal sperm morphology was 2.1% unit (95% CI = 0.7,3.5%) higher between men in the upper vs. lower half of unprocessed red meat intake ($p = 0.005$). Compared to non-consumers, men who consumed organ meat (median intake = 0.06 servings/week) had higher total sperm count ($p = 0.002$), concentration ($p = 0.03$),and progressive motility ($p = 0.005$). Conclusions: Our data suggest that unprocessed red meat is associated with higher percent morphological normal sperm.

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CORRELATES OF PAST YEAR DENTAL HEALTH VISITS AMONG BLACK MEN: FROM THE BLACK MEN'S HEALTH STUDY OF INDIANA. *Shauna Stapleton, Tracy Finlayson, Angelitta Britt, Lauren Parker, Haslyn Hunte (Purdue University, West Lafayette IN 47907)

Objective: This study aims to describe correlates of past year dental health visits among Black Men of Indiana. Methods: A 2011 health needs assessment was taken from a convenience sample of 1,444 Black men from 12 Indiana counties. Participants represented a wide range of socioeconomic backgrounds. Utilizing logistic regression analysis, compensating for clustering by county, predisposing and enabling factors were explored to determine their correlation to dental health visits within the previous year. Predisposing factors included age, sex, marital status, educational level, and employment status. Enabling factors included household income level, health insurance, place of sick care, smoking status, self-rated health, poor mental health days, social support, and fruit and vegetable servings per day. Results: Overall, 42% of the men surveyed had visited the dentist during the previous year. Preliminary analysis of the full model showed that those who were married (Odds Ratio (OR) = 1.34, $p < 0.01$), had a higher household income (OR = 1.83, $p < 0.05$), possessed health insurance (OR = 1.75, $p < 0.001$), had a usual place of sick care (OR = 1.42, $p < 0.05$), and consumed more fruit servings per day (OR = 1.81, $p < 0.05$) were significantly more likely to visit the dentist in the previous year. Rarely or never having social support (OR = 0.54, $p < 0.01$) had a significant negative association to dental health visits within the previous year. Conclusion: Correlations were found for both predisposing and enabling factors and should be considered when aiming to increase dental health visits among adult Black men during health promotion programs.

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THE ASSOCIATION OF METABOLIC SYNDROME AND ITS COMPONENTS WITH LOWER URINARY TRACT SYMPTOMS IN KOREAN MEN. *Soriul Kim, Heejin Kimm, Sun Ha Jee (Yonsei University Graduate School, Seoul Republic of Korea)

Lower Urinary Tract Symptoms (LUTS) are a common in elderly men. Though increasing evidence from epidemiologic studies indicates a relationship between LUTS and metabolic syndrome (MetS), their results are controversial. In this study, we investigated the relationship between MetS and its components and severity of LUTS in Korean men. This study included 4,445 Korean men aged 20 to 80 years old who participated in the Korean Cancer Prevention Study II (KCPS-II) from April 2004 to December 2007. The LUTS were assessed by the International Prostate Symptom Score (IPSS). The IPSS includes scores 3 questions on storage symptoms, 3 on voiding symptoms, and 1 on postmicturition symptoms. The presence of metabolic syndrome was defined using the updated National Cholesterol Education Program-Adult Treatment Panel III guidelines. The association between the severity of LUTS and MetS was presented as odds ratios (OR) and 95% confidence intervals (CI) estimated using logistic regression models. The presence of MetS was not associated with rate of moderate or severe LUTS (multivariate OR 0.94, 95% CI 0.81-1.09). Aging was observed to be a major risk factor for LUTS, such that men 60 years or older experienced 4-fold the odds of moderate or severe LUTS (OR 4.08, 95% CI 3.19-5.21) when compared with men 40 years or less. Component of MetS, such as low HDL cholesterol, has increased odds for moderate or severe voiding and postmicturition symptoms in multivariate analysis (multivariate OR 1.26 and 1.20, 95% CI 1.06-1.49 and 1.00-1.43, respectively). Our results suggested that the MetS is not associated with moderate or severe LUTS. However, we confirmed that low HDL cholesterol had favorable effects on higher sub-categorical LUTS, including voiding and postmicturition symptoms. (This study was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (14245 and 2011-0029348).)

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EXAMINING THE ASSOCIATION OF EVERYDAY DISCRIMINATION AND DEPRESSIVE SYMPTOMS IN BLACK MEN: THE SOCIAL SUPPORT FACTOR. *Angelitta Britt, Shauna Stapleton, Lauren Parker, Anita Ohmit, Haslyn Hunte (Purdue University, West Lafayette IN 47906)

Prior research suggests Blacks face a disproportionate heightened level of discrimination compared to some other racial groups. Discrimination has been associated with adverse mental health outcomes and disorders. Depression is noted as one of the most common mental health disorders in the United States. Although depression is a well-studied topic, literature specifically focusing on the factors and health effects associated with depression in Black men is sparse. This study examines the association between everyday discrimination and depressive symptoms and the influence of social support among Black men using data from the Indiana Black Men's Health Study, a health needs assessment study of 1,444 Black men in 12 Indiana counties. Results from ordinary least squares regression, suggests a positive significant association between everyday discrimination ($b = 0.130$, $p < 0.001$) and depressive symptomatology. Social support frequency was found to have a significant inverse effect ($b = -1.635$, $p < 0.001$) on depressive symptomatology. This analysis adds to the literature and provides insight on potential risk factors that may influence adverse mental health outcomes among Black men and suggest that a greater emphasis for social support in the Black community may assist in reducing the prevalence and health effects of depression.

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THE ILLNESS-DEATH MODEL TO STUDY PROGRESSION OF CHRONIC KIDNEY DISEASE. Julie Boucquemont, Benedicte Stengel, Marie Metzger, Georg Heinze, *Karen Leffondre (Univ. Bordeaux, ISPED, Centre INSERM U897-Epidemiologie-Biostatistique, Bordeaux France)

Chronic kidney disease (CKD) progression is usually assessed using measures of the glomerular filtration rate (GFR). If the event of interest is end-stage renal disease (ESRD), defined as a GFR<15mL/min/1.73m2, then the time-to-event is interval-censored between the last measurement when GFR>15mL/min/1.73m2 and the first measurement when GFR < 15mL/min/1.73m2. In addition, death is a competing event usually imposing censoring patients who die before ESRD diagnosis, at the time of last measurement (Model M1) or death (Model M2). Such choices of censoring times have been shown to produce biased effect estimates of exposures on the hazard of the event of interest. An alternative method is the illness-death model (IDM) for interval-censored data (Model M3) that accounts for the possibility to reachESRD between the last measurement and death. The objective is to evaluate whether M3 provides different effect estimates of known risk factors on the hazard of ESRD, as compared with M1 and M2. Among 704 patients at stage 3 CKD at baseline in the NephroTest cohort, 87 reached ESRD during follow-up and 78 died. All models included proteinuria, blood pressure (BP) and other known risk factors at baseline. For proteinuria, which was not associated with death, the estimates from M1 and M2 were either side of the M3 estimate (hazard ratio $HR_{M1} = 2.37$, $HR_{M2} = 2.95$ and $HR_{M3} = 2.54$). For high BP, which significantly increased the hazard of death after transition to ESRD (HR = 5.79), the estimate was lower with both M1 and M2 than with M3 ($HR_{M1} = 2.64$, $HR_{M2} = 2.83$ and $HR_{M3} = 3.18$), likely because M1 and M2 did not allow patients with high BP to reach ESRD before death. The IDM for interval-censored data allowingfor thisis likely toprovide better estimates than standard survival models for exposure associated with death, and avoids the need to makearbitrary choices regarding the censoring time to account for death as a competing event.

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A LATENT CLASS LINEAR MIXED MODEL TO INVESTIGATE TRAJECTORIES OF KIDNEY FUNCTION DECLINE.

*Karen Leffondre, Julie Boucquemont, Lucie Loubere, Marie Metzger, Benedicte Stengel (Bordeaux Segalen University, ISPED, Bordeaux France)

Chronic kidney disease (CKD) is characterized by progressive loss of kidney function, often measured by repeated assessments of the glomerular filtration rate (GFR). There is an increasing interest in identifying the different profiles of decline of GFR before or after end-stage renal disease (ESRD), and to investigate patient's characteristics associated with these trajectories. A latent class linear mixed model which has been used in other contexts allowed us to investigate such trajectories before ESRD in the ongoing NephroTest Study cohort. A total of 1793 patients with CKD stages from 1 to 5 at baseline were included. The number of annual measures of GFR (mGFR) per patient varied from 1 to 11, with a total of 580 patients who had at least three values of mGFR. We identified three classes of trajectories of mGFR over time, including 598, 864, and 331 patients, respectively. The mean trajectory within each class was found to be approximately linear with a slowly progressive decline over time. While the mean baseline value significantly differed from one class to the other (mean mGFR = 22.9, 42.9, or 61.7 mL/min/1.73m2, respectively), the slope of decline was of the same magnitude in each class.A multinomial logistic regression was used to determine patient's characteristics associated with each class membership. As expected, older patients orpatients with proteinuria at baseline were more likely to belong to the class with lower values of mGFR. In a sensitivity analysis, we found a further small class of patients (n = 49) who had a strong decline of mGFR over time. Smokers were more likely to belong to this class than to the other classes. This study illustrates how the latent class linear mixed model can be used to identify trajectories of renal function and their determinants.

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CHARACTERISTICS OF NEIGHBORHOODS IN WHICH DIALYSIS FACILITIES RESIDE MAY PREDICT FACILITY STANDARDIZED KIDNEY TRANSPLANT RATIOS.

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Although kidney transplant is the preferred treatment for end-stage renal disease (ESRD), 70% of prevalent U.S. ESRD patients are treated with dialysis. Dialysis facilities vary widely in their transplant rates. We investigated whether facility-level standardized transplant ratios (STRs) were associated with the characteristics of the neighborhoods in which the dialysis facilities were located. A total of 3983 facilities with an available STR from the Dialysis Facility Report (DFR) 2007-2010 data were geospatially linked to American Community Survey 2006-2010 data on census tract (neighborhood)-level sociodemographic factors. The association between neighborhood characteristics and STR was determined using linear mixed models with random intercepts for the neighborhoods and ESRD Networks, which regionally facilitate national quality of ESRD care initiatives. We adjusted for confounders previously found to be associated with facility STR [facility-level (percent black, mean age, percent with diabetes, CVD, and no pre-ESRD nephrology care, for- vs. not-for-profit, number of staff) and network-level (percent black, mean age, prevalent ESRD population size, and transplant centers per 10,000 ESRD patients)]. With full adjustment, we found that most neighborhood characteristics were associated with STR [β = change in STR associated with absolute 10% increase in exposure (95% CI)]: % crowded housing [-0.21 (-0.29,-0.13)], % unemployed [-0.15 (-0.18,-0.11)], % receiving public assistance [-0.12 (-0.14,-0.10)], % high school graduates [-0.11 (-0.09,-0.12)], % living in poverty [-0.08 (-0.09, -0.06)], % female head of household [-0.06 (-0.07,-0.04)], and % black [-0.03 (-0.04,-0.02)]. Each 0.1-increase in Gini index of income inequality (range, 0-1) was associated with a decrease of 0.05 in STR (95% CI, -0.08,-0.02). Facility neighborhood characteristics may be associated with kidney transplant rates, independent of facility and ESRD Network factors.

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THE KIDNEY DONOR RISK INDEX AND SURVIVAL BENEFIT OF DECEASED DONOR TRANSPLANTATION.

*Allan Massie, Dorry Segev (Johns Hopkins School of Medicine, Baltimore MD 21212)

The Kidney Donor Profile Index (KDPI), an index of risk of graft failure based on deceased donor risk factors, has been proposed as a tool for allocation of deceased donor kidneys; the KDPI score will be presented to surgeons as an aid in deciding whether or not to accept the offer of a donor organ. However, mortality on the kidney waitlist is high, and the survival benefit of kidney transplant with a high-KDPI kidney (high-KDPI KT) vs. waiting for a better offer is unknown. This retrospective cohort study of waitlist patients from 2002-2011 compared outcomes after high-KDPI transplantation to standard treatment (remaining on the waitlist or transplant with a lower-KDPI kidney) using time-dependent Cox regression, adjusting for transplant candidate characteristics. Outcomes were time-varying mortality hazard (time to decreased risk) and cumulative mortality (time to equal survival). Mortality risk increased in the first 30 days after high-KDPI KT, then decreased, becoming statistically significantly lower than standard treatment after 30 days (KDPI 71-80)/180 days (KDPI 81-90 and 91-100). Long-term (>3-year) mortality risk was lower after high-KDPI KT; the difference was statistically significant for KDPI 71-80 (HR = 0.78, 95% CI 0.70-0.86 p < = .001) but not for KDPI 81-90 (HR = 0.91, 95% CI 0.82-1.01, p = 0.1) or KDPI 91-100 (HR = 0.96, 95% CI 0.86-1.08, p = 0.5). Time to equal survival was 7.9 months post-transplant for KDPI 71-80, 17.7 months post-transplant for KDPI 81-90, and 20.2 months post-transplant for KDPI 91-100. Past these times, high-KDPI KT conferred a net survival advantage. High-KDPI KT confers net long-term survival advantage due to decreased mortality in the period 0.5-3 years post-transplant. High-KDPI KT is a viable treatment option for patients with end-stage renal disease.

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LONG-TERM RISK OF ESRD ATTRIBUTABLE TO LIVE KIDNEY DONATION: MATCHING WITH HEALTHY NON-DONORS.

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Following live kidney donation, higher rates of end-stage renal disease (ESRD) post-donation have been reported in African-American donors than in white donors, but no studies have compared ESRD incidence in donors to ESRD incidence in comparable non-donors. ESRD risk attributable to donation is unknown. We matched a cohort of 96217 live kidney donors (reported between 1994-2011) with replacement to 9364 healthy non-donor controls drawn from the NHANES study, using a previously published incrementally expanding radius matching algorithm based on age, gender, race, education, BMI, systolic blood pressure, and smoking history. We then linked both donors and controls to Center for Medicare/Medicaid Services data to obtain ESRD outcomes. Kaplan-Meier curves were used to compare 15-year ESRD incidence, overall and separately among racial/ethnic subgroups. A bootstrap was used to assess statistical significance. Results: Cumulative ESRD incidence at 15 years was 8× higher for live kidney donors (0.31%) than for healthy matched controls (0.04%, $p < 0.05$). Higher cumulative incidence was observed among donors than controls in every racial/ethnic group (2.3% vs. 0.0% among Causasians, 7.5% vs. 2.4% among African-Americans, 3.3% vs. 0.7% among Hispanics). Both among donors and among controls, African Americans had the highest incidence of ESRD, and Caucasians had the lowest incidence. Fifteen-year cumulative incidence was less than one percent among all racial/ethnic subgroups. Conclusions: Live kidney donors had higher rates of ESRD than matched controls, overall and across racial/ethnic subgroups. However, absolute risk of ESRD within fifteen years of donation is low in all subgroups.

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SYSTEMATIC DIFFERENCES AMONG ALCOHOL USERS: DO THEY APPLY IN NON-WESTERN POPULATIONS? EVIDENCE FROM THE GUANGZHOU BIOBANK COHORT STUDY. *Shiu Lun Au Yeung, Chaoqiang Jiang, Weisen Zhang, Tai Hing Lam, Kar Keung Cheng, Gabriel M Leung, C Mary Schooling (School of Public Health, Li Ka Shing Faculty of Medicine, the University of Hong Kong, Hong Kong SAR China)

Western observational studies show moderate alcohol use positively associated with health. Moderate alcohol users differ systematically from others, making these observations vulnerable to residual confounding. Observations from other contexts may help distinguish whether observations from western populations are confounded. To assess whether a Southern Chinese population would provide a more suitable setting to examine the association of moderate alcohol use with health, the authors examined differences between moderate and other alcohol users in this setting. The authors used multivariable, multinomial regression, adjusted for age and recruitment phase, to assess sex-stratified associations of alcohol use (never, occasional (<1/week), moderate (≤140g ethanol/week for women and ≤210g/week for men)) with health attributes and indicators in the Guangzhou Biobank Cohort Study (n = 26,361). The authors found occasional alcohol users had higher socio-economic position and better self-rated health, although more likely to be ever smokers and exposed to secondhand smoke than never or moderate alcohol users. Moderate alcohol users had lower socio-economic position and poorer health, particularly in men. Observations in alcohol epidemiology can be affected by residual confounding due to contextually specific systematic differences. Therefore, results from a particular setting should not be interpreted as causal unless verified in different populations, and if possible, in non-observational design.

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EVALUATING THE EFFECTS OF THE INTRODUCTION OF OFF-SALE ALCOHOL OUTLETS ON VIOLENT CRIME. *Daikwon Han, Dennis Gorman (Texas A&M University, College Station TX 77843)

Alcohol-related violence remains a significant problem in the United States. Despite the increasing evidence on the associations between alcohol availability and violence, there are still inconsistent findings on the effects of on- and off-sale outlets on violent crime. The aim of this study was to examine the effects on violence of a policy change that ended prohibition of off-sale alcohol outlets in Lubbock, Texas. We conducted times-series analysis of violent crime data from police records comparing the periods before (January 2006 –August 2009) and after (September 2009 – December 2011) the policy change. Autoregressive integrated moving average (ARIMA) intervention time-series models were used to assess the onset (abrupt or gradual) and duration (permanent or temporary) of the effects of the change in licensing policy on violent crime outcomes. Our results indicated that the effect of the policy change on both total violent crime and aggregated assault was small and did not approach statistical significant. Increased availability of alcohol through off-sale premises did not influence the type of violence reported to the police. These findings may support the view that the context within which drinking occurs is important in explaining the association between alcohol availability and acts of violence.

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USING PRESCRIPTION DRUG MONITORING DATA TO PREDICT PRESCRIPTION OPIOID MISUSE. *Deysia Levin, Denise Paone, Ellenie Tuazon, Emily Goldmann, Silvia Martins (Columbia University, New York NY 10032)

Aims: To identify possible predictors of elevated risk for "doctor shopping" – the practice of obtaining controlled substances from multiple health care practitioners without the prescribers' knowledge of the other prescriptions - a proxy for opioid analgesic misuse. Methods: The data used for this analysis is a subset of the New York State Prescription Drug Monitoring Program, and includes opioid prescriptions filled by 881,558 NYC residents in 2010. A case-control study design was utilized to identify those who met the criteria for doctor shopping, defined as visits to three or more practitioners and three or more pharmacies within a 3-month period. We randomly sampled controls who did not meet the criteria for doctor shopping. Controls were matched to cases on age category, gender, and borough in a 1:1 ratio, yielding a final analytic sample of 1,118 patients. A series of binomial logistic regressions were used to predict the odds ratio (OR) of doctor shopping for prescription-related variables, including type of opioid-analgesic, co-prescribing of certain opioid analgesics, and morphine equivalent dose. After exploratory analyses, a series of multivariate logistic models were constructed. Results: Univariate analyses showed that cases were 2.2 times more likely than controls to have prescriptions for Schedule II drugs (95% CI: 1.54-3.188), and that the greatest association with doctor shopping was receiving prescriptions for both oxycodone and hydrocodone (OR = 4.3; 95% CI: 2.83-6.66). Multivariate analyses yielded similar results, indicating that prescriptions for oxycodone and hydrocodone, and prescriptions for Schedule II drugs could be factors that increase the probability of doctor shopping (p <.0001). Conclusions: Using PDMP data, we identified possible predictors for opioid misuse. Patients with prescriptions for oxycodone or hydrocodone, and Patients with prescriptions for schedule II drugs are more likely to be a 'doctor shopper'. Keywords: opioids, prescription, abuse, doctor shopping

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STATE VARIATION IN UNDERREPORTING OF ALCOHOL INVOLVEMENT ON DEATH CERTIFICATES: MOTOR VEHICLE TRAFFIC CRASH FATALITIES AS AN EXAMPLE. *I-Jen Castle, Hsiao-ye Yi, Ralph Hingson, Aaron White (CSR Incorporated, Arlington VA 22201)

State variation in underreporting of alcohol involvement on death certificates has not been investigated in the literature. To examine the magnitude of underreporting in different states, we compared motor vehicle traffic (MVT)-related deaths identified from the Multiple Cause of Death (MCoD) data with decedents reported in national traffic census data from the Fatality Analysis Reporting System (FARS). Because no individual data linkage was available to us, we computed reporting proportion (RP) at the aggregate level as prevalence of any mention of alcohol-related conditions among MVT deaths in MCoD, divided by prevalence of decedents with blood alcohol concentration (BAC) test results (not imputed) ≥0.08% in FARS. Bivariate and multivariate analyses were conducted to explore state characteristics correlated with state RPs. Both MCoD and FARS identified about 450,000 MVT deaths in 1999-2009, with the RP as 16% for all deaths and 18% for vehicle driver deaths nationally. The RP did not improve over time, while prevalence of BAC ≥0.08% in MVT deaths increased slightly from 19.9% in 1999 to 24.2% in 2009. The RPs for decedents who were American Indian or Alaska Native, non-Hispanic, and ages 0-15 were higher than for other subpopulations. A large state variation in RP ranged from 2% (Nevada and New Jersey) to 81% (Delaware). State prevalence of driving after drinking too much was the only state characteristic robustly positively associated with state RP. These results encourage fostering completeness of death certificates, especially in states with very low RPs. Caution is merited when conducting state comparisons of alcohol-related mortalities using MCoD data.

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RECOVERY RESEARCH ON THE DRUG USE DISORDERS: WHO STARTS AND THEN QUITS EARLY? *Silvia Martins, Julian Santaella, Catalina Lopez-Quintero, Zila Sanchez, Jim Anthony (Columbia University, New York NY 10032)

Recovery from alcohol and other drug dependence syndromes is an important epidemiological topic, given increased prominence of these syndromes among global burdens of disease. To initiate epidemiological research on recovery and suspected determinants of persistence (and non-persistence) of first onset of drug dependence syndromes, we turned to cross-sectional data from recent National Surveys of Drug Use and Health (NSDUH, 2010-2011), with focus on an initial evidence for DSM-IV dependence recovery (i.e., having abstained from drug use for at least 30 days prior to survey assessment). The NSDUH nationally representative samples included many rapid-onset cases of alcohol dependence (AD; n = 400), cannabis dependence (CD; n = 433) or nonmedical use of prescription opioids dependence (POD; n = 256) among individuals who initiated use of these drugs 24 months before assessment. 21.8% of those with AD, 25.5% of those with CD and 49.0% of those with POD had recovered in the month prior to assessment. Multiple logistic regression models for complex sample survey data adjusted for demographics and other covariates, disclosed statistically robust associations as follows: (1) Alcohol: Among rapid-onset AD cases, statistically independent predictive associations with non-persistence (recovery) of AD included being 12-17 years old (vs. 18-25), African-American, Hispanic, Native American or Asian (vs. non-Hispanic Whites), female, and absence of using multiple drugs. (2) Cannabis: the only statistically independent predictive association with non-persistence (recovery) of CD was being 12-17 years old (vs. 18-25). (3) Prescription opioids: residing in more urban areas (vs. rural areas), and no recent history of depression (vs. recent history) were statistically independent predictors of non-persistence (recovery) of POD. Results suggest that there are substance-specific factors associated with early stages of recovery.

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GENDER DIFFERENCES IN EFFECT OF REDUCTION IN ALCOHOL USE ON HIV RISK BEHAVIOR IN TOMSK, RUSSIAN FEDERATION. *Ann C Miller, Viktoriya Livchits, Sidney Atwood, Adrienne Katrina Nelson, Shelly F Greenfield, Hilary Connery, Sonya Shin (Department of Global Health and Social Medicine, Harvard Medical School, Boston MA 02115)

Alcohol use disorders(AUD) are associated with lower tuberculosis(TB) treatment success and increased risk of development of drug resistance in TB patients with this comorbidity. AUDs are also known to increase sexually risky behavior. This analysis assesses the effect of reduction in alcohol use on HIV risk behavior in a randomized controlled trial of alcohol treatment in a TB hospital in Russian Federation. Methods: Patients were randomized to usual care, behavioral intervention(BCI), naltrexone (NTX) or both. Interviews at baseline, 3 and 6 months assessed addiction, behavior and socio-emotional factors, using Russian-adapted Risk Assessment Behavior(RAB) (HIV risk); Timeline-Follow-back calendars (alcohol use); and the CESD and Addiction Severity Index (depression, mental health, social factors). Missing data for 6 month visit was multiply imputed (MI). Baseline and 6 month responses were compared using ttests, rank sum or signed rank tests as appropriate. MI-adjusted association between changes in alcohol use and changes in HIV risk were assessed by Pearson's correlation. Results: Between 2007-2011 196 participants enrolled; 35(17.9%) females, 161(82.1%) males. Significant differences between female and male mean RAB scores at baseline were observed (female 3.5, male 4.4, $p = 0.04$). A statistically significant difference in mean RAB scores was observed across the cohort from baseline(4.3, range 1-13) to 6 months(3.4, range 1-7, $p < 0.001$). Study arm was not associated with RAB score change. Overall, there was no correlation between changes in heavy drinking days(HDD) per month and changes in RAB score($r = 0.01$). When this relationship was examined by gender, a reduction in HDD was moderately associated with a reduction in HIV risk behavior in women($r = 0.36$) but not in men($r = -0.01$). Conclusion: Interventions for alcohol treatment may affect HIV risk behavior differently in men and women in this setting. Gender specific interventions should be considered.

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SOCIAL PARTICIPATION AND DRUG USE IN A COHORT OF BRAZILIAN SEX WORKERS. *Hannah Leslie, Jennifer Ahern, Magda Chinaglia, Deanna Kerrigan, Sheri Lippman (University of California, Berkeley, Berkeley CA 94720)

Background: Structural interventions focused on community mobilization to engender an enabling social context have reduced sexual risk behaviors among sex workers. Interventions to date have increased social participation and shown an association between participation and safer sex. Although social participation could modify risk for other health behaviors, particularly drug use, research on structural interventions has not addressed this possibility. We assessed social participation and drug use before and after implementation of a clinical, social and structural intervention with sex workers intended to prevent sexually transmitted infections, including human immunodeficiency virus. Methods: We followed 420 sex workers participating in the Encontros intervention in Corumbá, Brazil, between 2003 and 2005. We estimated the association of participation in external social groups with drug use at baseline and follow-up using logistic regression and marginal modeling. Follow-up analyses of pre-/post-intervention change in drug use employed inverse probability weighting to account for censoring and were stratified by exposure to the intervention. Results: Social participation showed a protective association with drug use at baseline (1 standard deviation higher level of social participation associated with 3.82% lower prevalence of drug use, 95% confidence interval [CI] -0.15, 8.33). Among individuals exposed to Encontros, higher social participation was associated with an 8.58% lower level of drug use (95% CI 0.06, 23.33). No significant association was found among the unexposed. Conclusion: A structural intervention that modified sex workers' social environment, specifically participation in external social groups, was associated with reduced drug use. These novel findings suggest that sexual risk prevention initiatives that enhance social integration among marginalized populations can produce broad health impacts, including reductions in drug use.

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DSM-V NICOTINE USE DISORDER SYMPTOM PROFILES IN A REPRESENTATIVE SAMPLE OF THE LARGEST METROPOLITAN AREA IN SOUTH AMERICA. *João Mauricio Castaldelli-Maia, Laura Helena Guerra de Andrade, Maria Carmen Viana, Arthur Guerra de Andrade, Silvia Saboia Martins (Section of Psychiatric Epidemiology (LIM-23), Institute of Psychiatry, School of Medicine, Universidade de São Paulo (USP), São Paulo (SP), Brazil,)

Aims: Given the development of a new diagnostic classification(DSM-V) for nicotine use disorders(NUD), we aimed to identify continuous and cathegorical fenotipes among indivuduals who had at least 1 cigarette per week during lifetime. Most of the conceptual framework for NUD come only from alcohol use disorder(AUD) studies. Data came from São Paulo Megacity Project (SPM) collected between 2005-2007, which is part of World Mental Health Surveys. Methods: Exploratory factorial analysis(EFA) and latent class analysis(LCA) of the DSM-V NUD symptoms - SPM did not include the 3 DSM-IV nicotine abuse questions - were performed using Mplus software taking into account complex survey design features. Then, via weighted logistic regression models, we examined socio-demographic correlates of the DSM-V NUD latent classes. Results: As in DSM-V AUD studies, an one-factor model reached the best fit in EFA, including very high loadings(>60%) of all eight symptoms tested. The best LCA model was a four-class model: 1) a "non-symptomatic class"(31.1%), 2) a "lost control class"(27.3%) - defined by high probabilities of "use in larger amounts" and unable to cut down criteria-, 3) a "craving-tolerance class"(7.9%) and 4) a "high-symptomatic class"(33.6%). Those in the "lost-control class" and "craving tolerance class" were more than 2 times more likely to be 18-34 years-old than those in the non-symptomatic class. Being in the three symptomatic classes was associated with unemployment/other as compared being in the non-symptomatic class. Conclusion: Prevention and specific treatment protocol can be designed based on this data. Varenicline or bupropion, as anti-craving medications, seem to be an interesting treatment option for those in the "craving-tolerance class". Cognitive-behavioral therapy(plus pharmacological treatment) are adequate for those in "loss-control class". Unemployed and young adults could be the target of prevention interventions for NUD in Brazil.

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THE UTILITY OF THE ASSIST IN IDENTIFYING THE NEED FOR SUBSTANCE USE INTERVENTIONS AMONG AN INJURED EMERGENCY DEPARTMENT POPULATION. *Valerie Strezsak, Janette Baird, Christina Lee, Richard Longabaugh, Ted Nirenberg, Michael Mello (Brown University, Providence RI 02903)

The World Health Organization developed the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST V3.0) to screen for all levels of problem or risky alcohol and other substance use, based on use in the past three months. While developed for the primary care setting, the ASSIST is used in other settings, including emergency departments (EDs), to identify individuals who may benefit from a substance use intervention. We examined characteristics of a random sample of 684 injured ED patients who were screened with the ASSIST, received moderate or high alcohol scores, and agreed to take part in a telephone-based intervention for alcohol use. 533 (77.9%) scored between 11 and 26 for alcohol use, indicating the need for a brief intervention, and 151 (22.1%) scored between 27 and 39, indicating the need for more intensive treatment. 555 (81%) participants received a moderate or high score for at least one substance in addition to alcohol, indicating the need for an intervention, and 316 (56.9%) of them received moderate or high scores for two or more substances. The most common substances for which intervention was indicated were tobacco (478 [69.9%]), cannabis (329 [48.1%]), and cocaine (110 [16.1%]). In addition, many participants endorsed feeling ready to change their drinking (488 [72.2%]) and in the previous year reported having received some form of treatment for alcohol use (48 [14.7%]) and having sought out others to discuss their alcohol use (85 [26.1%]). These data suggest that the ASSIST can identify injured ED patients who would screen positive for recent substance use at levels indicative of the need for a brief intervention or more intensive treatment. ED patients who screen positive may also want to change their alcohol use but perhaps have not yet found adequate resources. Further study should include all ED patients and explore combined interventions for alcohol and other drugs as polysubstance use is common in this sample.

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INFLUENCES OF NEIGHBORHOOD SOCIOECONOMIC CHARACTERISTICS AND ALCOHOL AVAILABILITY ON DRINKING: RESULTS FROM THE MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS (MESA). *Allison Brenner, Ana Diez Roux, Luisa Borrell, Tonatiuh Barrientos-Gutierrez (Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor MI 48109)

Introduction: The residential neighborhood may influence alcohol use beyond individual factors (1), as exposure to neighborhood disadvantage may increase residents' stress, and alcohol use as a coping strategy (2). We examined whether neighborhood socioeconomic disadvantage and residential alcohol outlet density are associated with alcohol use. Methods: Data came from the Multi-ethnic Study of Atherosclerosis, a longitudinal study of 6,814 adults ages 45-84 years. We examined weekly and daily alcohol use, collected over 3-4 waves of the exam. Neighborhood disadvantage was assessed using 2000 census and 2005-2010 American Community Survey data, and liquor outlet density was computed based on commercially available food store data. We used nonlinear mixed models to test our hypotheses, and present only cross-sectional findings here. Results: Preliminary results indicate that the relationship between neighborhood factors and drinking depends on the type of alcohol consumed and drinking pattern. Residents of more disadvantaged neighborhoods had lower odds of heavy wine or hard liquor drinking (Odds Ratio (OR) = 0.77, $p < 0.01$; OR = 0.78, $p < 0.01$), but higher odds for heavy beer drinking (OR = 1.56, $p < 0.01$) and heavy daily alcohol use (OR = 1.34, $p = 0.05$) than residents of more affluent areas, adjusted for sex, race, exam year, income, education, occupation and marital status. Residents living in areas with a higher density of alcohol outlets had a 48% lower odds of heavier weekly drinking than residents in neighborhoods with lower alcohol outlet density ($p < 0.01$), adjusted for the same factors. Conclusions: Neighborhood disadvantage and the density of liquor stores influences alcohol use beyond individual-level risk factors. Results suggest that the relationship between disadvantage and drinking may depend on the specific alcohol. The inverse relation between outlet density and weekly drinking was not in the expected direction, and deserves further exploration.

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DIFFERENT PATTERNS OF ASSOCIATION BETWEEN ADULT SMOKING STATUS AND SMOKE-FREE HOME RULES IN TEXAS' BORDER AND NON-BORDER COUNTIES. *Oladimeji Akinboro, Allison Ottenbacher, Kim Linnear, Roderick Harrison, Marcus Martin, Thomas James, Eddilisa Martin, Jim Murdoch, Avani Parikh, Kathryn Cardarelli (University of North Texas Health Science Center, Fort Worth TX 76107)

Secondhand smoke (SHS) is associated with lung cancer, heart and respiratory diseases. SHS exposure occurs most commonly in homes and workplaces, and having smoke-free home rules has been shown to reduce SHS exposure. We examined the association between adult smoking status and home smoking rules in 6 counties in Texas, as a part of the evaluation of a Centers for Disease Control and Prevention (CDC)-funded community transformation grant. Counties included a mix of urban non-border, rural non-border, urban border, and rural border counties. At least 385 adults from each county were selected using a probability-based dual-frame random digit dial sampling technique and surveyed via computer-assisted telephone interviews between September and November 2012. Survey sampling weights correcting for the sample design, non-response, and post-stratification, were applied in obtaining the population-based odds ratio (OR) estimates and confidence intervals (CIs) for each county, after adjusting for age, gender, race/ethnicity, and education. In the non-border counties, current smokers were less likely than those who have never smoked to have smoke-free home rules with ORs and 95% CIs of 0.14 (0.06, 0.32) and 0.28 (0.11, 0.71) in the urban non-border counties, and 0.17 (0.07, 0.43) and 0.15 (0.06, 0.39) in the rural non-border counties. However, in the two border counties with very high Hispanic populations (87% and 96%), no association was seen between current smoking and having smoke-free home rules, irrespective of whether it was urban (OR = 0.49; 95% CI = 0.21, 1.14) or rural (OR = 0.53; 95% CI = 0.20, 1.43). This suggests that while smoke-free home campaigns targeting current smokers may be effective in the non-border counties, different targets may be appropriate in the border counties. In summary, smoke-free home interventions should take into consideration, the socio-geographical features of different environments, in designing effective campaigns.

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THE RELATIONSHIP BETWEEN PERCEIVED DISCRIMINATION AND THERAPEUTIC AND ILLICIT DRUG MISUSE IN CHICAGO, IL. *Haslyn Hunte, Tracy Finlayson (Purdue University, West Lafayette IN 47906)

Based on several stress-coping frameworks, recent studies have suggested that perceived experiences of discrimination, a psychosocial stressor, may be associated with various risky health behaviors. The 2001 Chicago Community Adult Health Study (n = 3,105), a face-to-face representative probability sample of adults in Chicago, Illinois, was used to examine the relationship between lifetime everyday discrimination, major discrimination, and the use of illicit and therapeutic drugs for nonmedical reasons. We used negative binomial logistic and multinomial regression analyses controlling for potential confounders. Approximately 17% of the respondents reported using one or more illicit drugs and/or misusing one or more therapeutic drug. Adjusting for socio-demographic characteristics, other stressors and various personality related characteristics, results from negative binomial regression suggest that respondents who experienced moderate to high levels of everyday discrimination misused on average 1.5 different kinds of drugs more than respondents that experienced relatively low levels of everyday discrimination ($p < 0.05$). Similarly, an increase in one lifetime major discrimination event was associated with an increase of misusing 1.3 different drugs on average regardless of experiences of everyday discrimination ($p < 0.001$). When examining the types of drugs misused, results from multinomial logistic regression suggest that everyday discrimination was only associated with illicit drug use alone, however lifetime major discrimination was associated with increased odds of using any illicit and both illicit/therapeutic drugs. Mental health and substance use clinical providers should be aware of these potential relationships and consider addressing the harmful effects of perceived discrimination, in all patients not only among racial/ethnic minority patients.

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BEYOND INTENTION-TO-TREAT: A DEEPER UNDERSTANDING OF ADHERENCE-BASED ANALYSES. *Jay Kaufman (McGill University, Montreal QC Canada)

Most methodologists recommend intention-to-treat (ITT) analysis in order to minimize bias when assessing treatment effectiveness. Although an unbiased estimator for the causal effect of treatment assignment, the ITT estimator is biased for the actual effect of receiving treatment. Alternatives to the ITT analysis have become increasing popular, including Per Protocol, As Treated, Average Causal Effect, and Complier Average Causal Effect analyses. The purpose of this symposium is 1) review these different approaches, and 2) illustrate the similarities, differences, and underlying assumptions so that the appropriate analysis is matched to the appropriate context. Dr. Shrier will provide an overview of ITT, Per Protocol, As Treated analyses, and Complier Average Causal Effect calculated through Principal Stratification or Instrumental Variable analyses, illustrating underlying assumptions and limitations using two data sets from the literature. Dr. Steele will explain Principal Stratification in greater depth. Using causal diagrams and simulations, he will illustrate how a broader view of this method could improve its clinical relevance. Dr. VanderWeele will expand on the discussion and illustrate the implications when some of the underlying assumptions fail. Particular attention will be paid to the exclusion restriction assumption, and the effect of dichotomizing adherence when it is really a multi-level variable.

Speakers:

1. *Causal approach to adherence-based analysis: Is it really new?*, Ian Shrier, Center for Clinical Epidemiology, McGill University.
2. *Principal Stratification for adherence-based analyses: a new birthday suit for the emperor?*, Russell J. Steele, Department of Mathematics and Statistics, McGill University.
3. *Implications when the assumptions fail: What does it all mean?*, Tyler VanderWeele, Department of Epidemiology, Harvard School of Public Health, Harvard University.

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NEW METHODS FOR AN OLD EPIDEMIOLOGIC PROBLEM: AGE, PERIOD, AND COHORTS EFFECTS. *Whitney Robinson, Katherine M Keyes (University of North Carolina, Chapel Hill NC 27599)

Age-period-cohort (APC) methods are used to model three important drivers of population trends in health. However, use of APC methods has been stymied for decades by an identification problem. Specifically, given any two effects (age, period, or cohort), the third effect is determined (i.e., Cohort = Period – Age). Therefore, with standard approaches, it is impossible to disentangle how each effect uniquely contributes to population trends. Various methods have been devised to work around this problem, but the results were sensitive to questionable assumptions required by each method. Recently, statistical advances have re-invigorated APC analysis in the epidemiological and sociological literature. Applications of hierarchical models, principal components regression, and median polish have enabled researchers to gain insight into important drivers in population health. In addition, innovative conceptual work has better defined the meanings underlying age, period, and cohort effects using theoretical frameworks, such as the potential outcomes and lifecourse theory. The speakers in this symposium will illustrate recent statistical advances using applied examples, such as trends in obesity prevalence and cancer incidence and mortality. The symposium will also illustrate new conceptual insights into the utility of APC analysis. The symposium will conclude with discussion from Dr. Theodore Holford, who has pioneered methods for assessing APC effects for more than thirty years.

Speakers:

1. *A potential-outcomes causal framework for age-period-cohort analysis* - Etsuji Suzuki, PhD (Okayama University).
2. *Hierarchical age-period-cohort models: overcoming the limitations of conventional linear models* - Yang Yang, PhD (UNC, Chapel Hill).
3. *A life course approach to age-period-cohort methods* - Whitney Robinson, PhD (UNC, Chapel Hill).

Discussant: Theodore R. Holford, PhD (Yale University).

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OLD STUDIES, NEW QUESTIONS: MAXIMIZING THE UTILITY OF EXISTING DATA AND THE BIASES THAT CAN RESULT. *Polly Newcomb (Fred Hutchinson Cancer Research Center, Seattle WA 98195)

Recruiting participants into epidemiologic studies takes time and money. As a result, epidemiologists must often be creative in finding ways to repurpose existing studies and administrative databases to evaluate new hypotheses. This means finding ways to leverage data that has already been collected to address research questions that those data were not originally designed to address Although such repurposing of data collected for other purposes can be an efficient tactic to extending our inferences, this approach may be challenging and can sometimes be burdened by missing data and biases. To enhance opportunities and limit challenges, researchers should consider augmenting existing data sources. In this session we will explore methods to get the most valid information for a new study, using old(er) data. Session participants include investigators who have expanded and enhanced old studies, as well as researchers who have identified the problems in these approaches.

Speakers:

1. *Expanding a cohort study: adding family members and body parts!* - Sue Hankinson (UMASS Amherst, HSPH).
2. *New insights from mature studies: The modern epidemiology consortium* - Patricia Hartge (NCI).
3. *Changing perspective: turning a retrospective study into a prospective cohort* - Amanda Phipps (FHCRC).
4. *Using external validation studies to quantify the magnitude of confounding by an unmeasured covariate* - Til Sturmer (UNC).

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RECORDING NATURE'S ANSWERS: MEASUREMENT BIAS IN EPIDEMIOLOGY. *Jessie Edwards, Elizabeth Ogburn (University of North Carolina, Chapel Hill NC 27599)

Measurement error is pervasive in epidemiology. While errors in exposures, confounders/modifiers, and outcomes may bias the results of epidemiological analyses, quantitative methods to account for such bias are infrequently used. Reticence to address measurement error in epidemiologic analyses could stem from the assumptions required to use traditional measurement error techniques or the lack of flexibility in these techniques to incorporate confounders/modifiers, time-varying covariates, or time-to-event data. Accounting for measurement error in the design of epidemiologic studies, using repeated measurements or an internal validation study, is advantageous when using these methods, though external validation data or assumed values of sensitivity and specificity can be used as well. The speakers in this symposium will present methods to address exposure measurement error, covariate measurement error, and outcome misclassification in various epidemiologic analyses and illustrate these methods using important applications. Specifically, speakers will 1) discuss the effects of measurement error in confounders and mediators, as well as use 2) maximum likelihood and 3) Bayesian methods to account for measurement error. The symposium will remove barriers to accounting for bias due to measurement error by demonstrating how measurement error techniques can be applied in a wide range of epidemiologic settings.

Speakers:

1. *Analytic Results on Bias Due to Nondifferential Misclassification* - Elizabeth Ogburn (Harvard School of Public Health).
2. *Methods to account for misclassification of cause-specific mortality* - Jessie Edwards (UNC Gillings School of Global Public Health).
3. *Bayesian adjustment for exposure misclassification* - Paul Gustafson (University of British Columbia).

Discussant: Enrique Schisterman, NICHD/NIH.

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TEACHING INTRODUCTORY EPIDEMIOLOGY: NECESSARY SIMPLIFICATIONS VS. PERPETUATING MYTHS. *Penny Howards, Tim Lash (Emory University, NC 30322)

When teaching introductory epidemiology, it is sometimes necessary to simplify complex concepts for students new to the field. Without these compromises, students may be overwhelmed by nuances and exceptions, and may consequently lose sight of the larger message. These simplifications are ordinarily rectified by further study. There is, however, a danger that oversimplified concepts will lead to inappropriate applications in the field or incorrect interpretation of results, especially among individuals who only take an introductory class. By way of example, introductory-level teaching may lead students to believe that non-differential misclassification always biases estimates of association to the null, that the attributable fraction estimates the probability that an exposed person's disease was caused by the exposure, and that case-control odds ratios can only estimate the risk ratio when the disease is rare. Students new to the field may not fully comprehend the more nuanced discussions of these topics, so presenting them clearly and with sufficient detail in an introductory course is a challenge. In this symposium, we will weigh compromise against completeness as approaches to presenting concepts that are commonly simplified at their first introduction to epidemiology students.

Speakers:

1. *Perspectives on Teaching Retrospective and Prospective Designs* - Timothy L. Lash, Emory University School of Public Health.
2. *How to Teach Case-Control Studies in Introductory Courses, Without Any Reference to the Rare Disease Assumption* - Jan P. Vandenbroucke, Leiden University Medical Center.
3. *Risk: The Abridged and Unabridged Versions* – Miguel A. Hernán, Harvard School of Public Health.

Discussant: Daniel R Brooks, Boston University School of Public Health.

L01

USING ASYMMETRY IN FAMILY HISTORY TO PROBE GENETIC MECHANISMS: APPLICATION TO THE GENETICS OF BREAST CANCER. *Clarice Weinberg, Min Shi, Lisa DeRoo, Jack Taylor, Dale Sandler, David Umbach (National Institute of Environmental Health Sciences, Research Triangle Park NC 27709)

Epidemiologic evidence suggests the prenatal environment may influence breast cancer risk; the mother's genome may have effects through its influence on that environment. A recent report of a parent-of-origin effect from a family-based Icelandic breast-cancer study (Kong, et al. Nature 462: 868-74, 2009) suggests that genetic imprinting also plays an etiologic role. Both of these little-studied mechanisms would tend to produce asymmetry in family histories, e.g. with more breast cancer in maternal than in paternal lineages. Using models with either maternal genetic effects or imprinting effects, we calculate the relative risk for maternal versus paternal grandmothers. For diseases not limited to one sex, we also compute the relative risk retrospectively in mothers versus fathers of affected offspring, and the relative recurrence risks in offspring of affected mothers versus affected fathers. We apply these ideas to a study of breast cancer. Our Sister Study cohort includes 50,844 women, each of whom was the sister of a woman with breast cancer. Based on 32,923 distinct families where the participant was a full sister of a case and reported data for both grandmothers, 5,039 reported that exactly one of the two had breast cancer. Using those discordant pairs we estimated the maternal/paternal grandmother relative risks in strata defined by the youngest age at diagnosis of a sister in the family. Overall the relative risk was skewed toward maternal grandmothers. This skewing was strongly related to the age at diagnosis of the granddaughter case, peaking for cancers occurring around the time of menopause, in the age decade 45-54. While we cannot exclude self-selection bias, these data suggest that breast cancer occurring near the time of the menopausal transition may be influenced either prenatally by maternal genes or later through gene variants that preferentially express the maternal copy.

L02

DIETARY FLAVONOID INTAKE AND RISK OF BARRETT'S ESOPHAGUS. *Jessica Petrick, Susan Steck, Patrick Bradshaw, Lawrence Engel, Ka He, Thomas Vaughan, Marilie Gammon (University of North Carolina-Chapel Hill, Chapel Hill NC 27599)

Flavonoids are bioactive polyphenolic compounds that are concentrated in fruits and vegetables and have been shown in laboratory experiments to have chemotherapeutic effects against Barrett's esophagus (BE), a precursor lesion for esophageal adenocarcinoma. However, no epidemiologic studies to date have examined whether flavonoids are associated with BE incidence. We examined our hypothesis that dietary flavonoid intake is inversely associated with risk of developing BE using data from a case-control study in western Washington state. BE cases (n = 170) and individually matched controls (n = 183) completed a self-administered, validated 131-item food frequency questionnaire (FFQ). To estimate flavonoid intake, we developed a flavonoid-specific database by linking each FFQ item on frequency of dietary intake and portion size (in the year prior to diagnosis) with existing databases of food-specific flavonoid content from the U.S. Department of Agriculture. Estimated mean intake of total flavonoids, for which black tea, orange juice and wine were the largest dietary sources, was 125.03 mg/day among controls and 123.55 mg/day among cases. In logistic regression models adjusted for age, sex, body size and kilocalories, risk of BE (specialized intestinal metaplasia) was reduced by 51% in relation to intake of anthocyanidins, for which wine, bananas and fruit juice were the major dietary sources (Odds Ratio = 0.49, 95% Confidence Interval: 0.30-0.80, for quartiles 2-4 combined vs. quartile 1). More modest decreases were noted for flavanone, flavonol, isoflavone, and lignan intakes. A modest increased risk was observed for flavones, of which the main dietary source in this population was pizza. Our finding of an inverse association between anthocyanidins and BE risk, which require replication, suggests that dietary intake of these compounds may be a risk reduction strategy for this precursor lesion.

L03

MIGRAINE AS A RISK FACTOR FOR BREAST CANCER: IS THERE ETIOLOGIC HETEROGENEITY? *Min Shi, Lisa DeRoo, Dale Sandler, Clarice Weinberg (NIEHS, Research Triangle Park NC 27709)

Breast cancer and migraine headache share the feature that some cases are influenced by hormones. Some but not all studies reported an inverse association between migraine and risk of breast cancer but none distinguished menstrual (which tends to be timed with the menstrual cycle) from non-menstrual migraine. To examine the association between migraine and breast cancer, we used the Sister Study, a cohort study of 50,884 women whose sister had breast cancer, and the Two Sister Study, a sister-matched case-control study of 1,442 breast cancer cases (diagnosed before age 50). We analyzed the two studies individually and also pooled via a hybrid Cox model. We examined subtypes of cancer (invasive versus *in situ*, estrogen-receptor/progesterone-receptor (ER/PR) status) and menstrual and non-menstrual migraine. Overall analysis did not show an association between breast cancer and history of migraine and did not confirm the previously reported inverse association between migraine and ER + /PR+ invasive breast cancer. We found an inverse association between migraine history and ductal carcinoma *in situ* in the Sister Study (hazard ratio = 0.54, 95% CI (0.34, 0.85)) but this did not replicate in the Two Sister Study (OR = 1.14, 95% CI (0.58, 2.26)). While there was no overall association between migraine and ER-/PR- cancer, in both studies women with non-menstrual migraine had increased risk while women with menstrual migraine had decreased risk (combined-analysis OR = 1.47, 95% CI (1.03, 2.83) for non-menstrual migraine, OR = 0.68, 95% CI (0.43, 1.05) for menstrual migraine). In a case-only analysis of invasive breast cancer, menstrual migraine was associated with hormone receptor positive cancer and nonmenstrual migraine with hormone receptor negative cancer (heterogeneity p = 0.02). Hormone-sensitive migraine may be a biomarker indicating a predisposition to hormone-sensitive breast cancer.

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L04

THE HYGIENE HYPOTHESIS AND THE RISK OF PEDIATRIC CROHN'S DISEASE. *Vicky Springmann, Paul Brassard, Alfreda Krupoves, Devendra Amre (University of Montreal, Ste-Justine Pediatric Hospital Research Center, Montreal QC Canada)

The incidence of pediatric Crohn's disease (CD) is on the rise. Multiple genetic loci explain <15% of the disease variance, indicating a role for environmental factors. The Hygiene Hypothesis (HH) stipulates that sanitary conditions prevailing in developed countries prevent exposure to antigens early in life, precluding immunological tolerance and resulting in abnormal immunological responses with subsequent exposures. Although well established for other phenotypes, the role of the HH in CD remains unclear. Objective: To assess whether frequency, timing and type of childhood infections are associated with risk of pediatric CD. A case-control study was performed, including cases of CD consecutively diagnosed at a pediatric hospital from 1983-2005. Controls were selected from the provincial medical insurance database and matched to the cases for age, gender, geographical location and period of insurance coverage. Infection exposure was ascertained using the International Classification of Diseases codes, recorded by physicians after each medical visit. Conditional logistic regression analysis accounting for potential confounding variables (number of medical visits, family income) was used. Odds ratios (OR) and corresponding 95% confidence intervals (95% CI) were estimated. The study population comprised of 409 cases and 1621 controls. Adjusted conditional logistic regression analysis suggested that infection exposures prior to disease diagnosis were associated with reduced risks for CD (OR = 0.71, 95% CI = 0.51-0.98, p = 0.037). The risk reduction was attributable to infection exposures primarily during the first 5 years since birth (OR = 0.74, 95% CI = 0.57-0.96, p = 0.025) and to infections affecting the kidney and urinary tract (OR = 0.65, 95% CI = 0.99-1.55, p = 0.056). Our study provides support for the HH in CD whereby exposure to infections in early childhood can reduce risks.

L05

A PROSPECTIVE STUDY OF CONSTIPATION, LAXATIVE USE, AND RISK OF COLORECTAL CANCER. *Jessica Citronberg, Elizabeth Kantor, Emily White (Fred Hutchinson Cancer Research Center - Public Health Sciences Division, Seattle WA 98109)

Constipation and laxative use have been hypothesized to increase colorectal cancer (CRC) risk, but existing epidemiological studies have been inconclusive The authors prospectively examined the association between colorectal cancer and constipation, chemical laxative use, and fiber laxative use among 69,778 participants of the Vitamin and Lifestyle (VITAL) study. Questionnaires were used to ascertain average 10-year chemical laxative use, fiber laxative use, and constipation. Individuals were followed from the time baseline questionnaire was received (2000-2002) until 2008 for CRC incidence, over which time 507 incident CRC cases occurred. Cox proportional hazard models were used to estimate the multivariate-adjusted hazard ratios (HRs) and 95% confidence intervals (95% CI). Compared to individuals who used chemical laxatives less than once per year, the HRs associated with low (1 – 4×/year) and high (≥5×/year) use were 1.49 (95% CI = 1.04-2.14) and 1.43 (95% CI = 0.82-2.28), respectively (Ptrend = 0.05). Multivariate-adjusted HRs for CRC were significantly decreased and lowest in individuals who reported using fiber laxatives often (>2 days/week) versus those who reported no use (HR = 0.44, 95% CI = 0.21-0.95), although the trend was not significant (Ptrend = 0.19). No statistically significant associations between constipation and CRC were observed. Findings from this study suggest that risk of CRC increases with chemical laxative use and decreases with fiber laxative use. As such, for the treatment of constipation, fiber laxatives should be considered instead of chemical laxatives.

L06

POLYMORPHISMS IN VITAMIN D-RELATED GENES AND RISK OF UTERINE LEIOMYOMATA. *Lauren A Wise, Edward Ruiz-Narvaez, Lynn Rosenberg, Steve Hadded, Julie R Palmer (Slone Epidemiology Center, Boston University, Boston MA 02215)

Background: The incidence of uterine leiomyomata (UL) is 2-3 times higher in black women than white women. Lower vitamin D levels have been hypothesized to contribute to the racial disparity, but data to support this hypothesis are scarce. Vitamin D receptors are found in uterine tissue and vitamin D inhibits proliferation of UL cells in vitro. A recent cross-sectional study found lower serum vitamin D3 levels in UL cases than controls. Methods: We examined the risk of UL in relation to twenty polymorphisms in genes involved in vitamin D metabolism: six in *VDR*, five in *GC*, four in *CYP2R1*, two in *NADSYN1*, two in *CYP24A1*, and one in *CYP27B*. Using already-genotyped samples from the Black Women's Health Study, a prospective cohort study, we identified 197 incident UL cases (diagnosed during 1997-2011) and 481 controls (no UL diagnosis through 2011). All women were premenopausal, had intact uteri, and were aged 23-50 years in 1997. Associations of polymorphic variants with UL risk were assessed using logistic regression with control for age and percent European ancestry. Results: Four polymorphisms were associated with UL risk at the nominal significance level of $p < 0.05$ (rs10766196 in *CYP2R1*, rs12800438 and rs4944957 in *NADSYN1*, and rs73913755 in *CYP24A1*). After correction for multiple hypothesis testing, only one polymorphism remained statistically significant (rs10766196 in *CYP2R1*): relative to the AA genotype (most prevalent), the odds ratio was 1.51 (95% confidence interval (CI) = 1.03, 2.21) for the AG genotype and 4.97 (95% CI = 1.87, 13.4) for the GG genotype (corrected P-trend = 0.019). The G allele of rs10766196 has been associated with lower vitamin D levels in previous studies. Conclusions: Our data support the hypothesis that the vitamin D pathway is involved in UL etiology. A prospective study involving direct measurement of vitamin D levels in cases and non-cases is warranted.

L07

RISK OF CARDIAC EVENTS IN OLDER MEN RECEIVING TESTOSTERONE REPLACEMENT THERAPY. *Jacques Baillargeon (University of Texas Medical Branch, Galveston TX 77555)

Background: Androgen treatment for older men has increased substantially over the past decade. There is concern that androgen treatment increases the risk of cardiac events. Objective: To examine the risk of cardiac events (myocardial infarction [MI] resulting in hospitalization, coronary artery bypass graft [CABG], or percutaneous transluminal coronary angioplasty [PTCA]) in a population-based cohort of older men receiving intramuscular TRT. Methods: Using a 5% national sample of Medicare beneficiaries, we identified 6,160 patients treated with at least one injection of androgen therapy between January 1, 1997 and December 31, 2005. We matched this cohort to 18,480 androgen nonusers at a 1:3 ratio, on age at initial drug administration, race, Medicaid eligibility, and an MI prognostic index score. Patients were followed until December 31, 2005, or until they lost coverage from Medicare Parts A and B, enrolled in a health maintenance organization, experienced a cardiac event or died. Results: Receipt of intramuscular androgen treatment was not associated with an increased risk of the combined outcome of MI, CABG, or PTCA (HR = 1.04 95% CI, 0.91-1.18). Moreover, the risk of a cardiac event did not increase with cumulative dose of androgen received in the first year of treatment. Conclusions: Older men who are treated with intramuscular testosterone do not appear to have a statistically significant increase in cardiac events. Future population-based studies, particularly those assessing newer formulations of androgen treatment, should be conducted to further examine this risk.

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L08

OBSTRUCTIVE SLEEP APNEA AS A RISK FACTOR FOR SILENT CEREBRAL INFARCTION. *Eo Rin Cho, Hyun Kim, Hyung Suk Seo, Sooyeon Suh, Seung Ku Lee, Chol Shin (Institute of Human Genomic Study, Korea University College of Medicine, Republic of Korea)

Previous studies have suggested that obstructive sleep apnea (OSA) may be a risk factor for stroke. In this study, we assessed that OSA is an independent risk factor of silent cerebral infarction (SCI) in the general population, and in a non-obese population. This study recruited a total of 746 participants (252 men and 494 women) aged 50-79 years as part of the Korean Genome and Epidemiology Study (KoGES); they underwent polysomnography, brain magnetic resonance imaging and health screening examinations. SCI was assessed by subtypes and brain regions, and lacunar infarction represented lesions <15 mm in size in the penetrating arteries. Moderate-severe OSA was determined by apnea-hypopnea index ≥15. The results indicated that 12.06% had moderate-severe OSA, 7.64% of participants had SCI and 4.96% had lacunar infarction. Moderate-severe OSA was associated positively with SCI [odds ratio (OR): 2.44, 95% confidence interval (CI): 1.03-5.80] and lacunar infarction (OR: 3.48, 95% CI: 1.31-9.23) in the age ≥65-year group compared with those with non-OSA. Additionally, in the basal ganglia, OSA was associated with an increase in the odds for SCI and lacunar infarction in all age groups, and especially in the ≥65-year age group. In the non-obese participants, OSA was also associated positively with SCI in the ≥65-year age group, lacunar infarction in all age groups, and especially in the ≥65-year age group. There was also a positive association with the basal ganglia. Moderate-severe OSA was associated positively with SCI and lacunar infarction in elderly participants. Treatment of OSA may reduce new first-time cerebrovascular events and recurrences.

L09

BYPASSING FIRST LEVEL CLINICS FOR CHILDBIRTH IN RURAL TANZANIA: A CENSUS OF 3000 RECENT DELIVERIES. *Sabrina Hermosilla, Margaret Kruk, Elysia Larson, Godfrey M Mbaruku (Columbia University, New York NY 10032)

Background: National maternal mortality reduction strategies in low-income countries rely on primary care expansion. We assessed delivery care utilization patterns among women in rural Tanzania to measure the extent, determinants, and results of bypassing local clinics for secondary care (health center or hospital). Methods: We conducted a census of all deliveries between 6 weeks - 12 months in 24 rural clusters in Pwani Region, Tanzania. We assessed women's demographic and obstetric characteristics, quality of their birth experience, and local clinic functioning through structured assessments. We analyzed characteristics associated with bypassing primary care clinics using logistic regression (robust standard errors). We examined differences between bypassers' and non-bypassers' birth experiences in bivariate analyses. Findings: We interviewed 3,019 eligible women (93% response rate). The population was 25.7% first time mothers and 75.1% literate. 71.0% delivered in a health facility, of which 41.8% bypassed primary care to deliver in a health center or hospital. The bypassing likelihood increased with primiparity (OR (odds ratio) 2.5, $p < 0.001$), perceived poor quality at the local clinic (OR 1.3, $p = 0.046$), and decreased with recent clinic renovations (OR 0.39, $p = 0.017$) and clinic performance of 4 or more obstetric signal functions (OR 0.19, $p < 0.001$). Bypassers reported greater receipt of mother and newborn exams and better quality of care. Interpretation: Bypassing first level clinics for obstetric care is common among women in eastern Tanzania. First birth and poor quality of care at the local clinic appear to be major determinants of bypassing. Women who delivered at hospitals and health centers reported better quality of care. Primary care is not meeting the expectations of women in this rural low-income setting, problematizing its role as a strategy for reducing maternal mortality in Africa.

L10

TREATMENT DECISION-MAKING IN VETERANS WITH EARLY STAGE PROSTATE CANCER. *Soe Soe Thwin, Kerri Clough-Gorr, Sanjay Raju, Nicole Kosik, Kelly Cho, John Hermos, Michael Gaziano (VA-Boston Healthcare System, Boston MA 02130)

Background: Prostate cancer is the second leading cause of cancer death for men in the US. Similar long term survival rates and functional capacity across different therapies have been reported, but little is known about factors related to therapy decision-making. Objective: We conducted this study to evaluate correlates of treatment decision making in a cohort of US veterans diagnosed with early stage prostate cancer. Methods: We analyzed data from an observational cohort of 921 veterans who were diagnosed with early stage prostate cancer (T0-T3, less than stage D), between 1999 and 2006 at 16 VA centers. We compared demographic and clinical characteristics across therapy type (radical prostatectomy, radiation, observation, and other). Logistic regression methods were employed to determine factors associated with type of therapy received within 2 years of diagnosis. Results: Therapies administered were 30% radical prostatectomy, 44% radiation, 17% observation, and 9% other. Younger age and being comorbidity-free at diagnosis were significantly related to receipt of radical prostatectomy, Odd Ratio(Confidence Interval) = 3.2(2.2-4.7)and 1.8(1.3-2.4) respectively. Moreover, odds of receiving prostatectomy instead of radiation increased if the veteran was both young and comorbidity free. Marital status played an important role in receipt of radical prostatectomy versus other therapies in the very young (<55years) age group. Race, education, family history, psa level, or methods of detection were not determinants of therapy after adjusting for age, comorbidity and marital status. Conclusion: Understanding the interplay between demographic and clinical factors related to treatment of early stage prostate cancer remain an important issue for Veterans Administration which provides health care to approximately 8.7 million veterans annually, 60% of whom are men over 60 years of age.

L11

PATTERNS IN SCREENING MAMMOGRAPHY UTILIZATION BY SOCIO-DEMOGRAPHIC AND BREAST CANCER RISK FACTORS BETWEEN 2000 AND 2012. *K Bolton, J Mace, B Geller, B Sprague (University of Vermont, Burlington VT 05401)

Over the past decade there has been extensive scientific and media controversy regarding mammography screening in the United States, highlighted by changing screening recommendations, concerns about over-diagnosis, and calls for risk-based screening. The impact of this public debate on patterns in mammography utilization is poorly understood, particularly in regard to trends in screening utilization according to patient sociodemographic and risk factors. We examined trends in patient characteristics between 2000 and 2012 using data from the Vermont Breast Cancer Surveillance System (VBCSS). The VBCSS includes a statewide registry of all screening mammography performed in Vermont, including data collected directly from both patients and clinic staff. We examined the distributions of age, educational attainment, and breast cancer risk factors (including family history of breast cancer and previous history of breast biopsy) among women aged 40 and over receiving screening mammograms, by calendar year. Between 2000 and 2012, the proportion of college-educated patients increased from 37.9% (95% CI: 37.5, 38.4) to 48.5% (95% CI: 47.9, 49.1), with over half (5.4; 95% CI: 4.6, 6.1) of the percentage increase occurring between 2009 and 2012. The percent of patients reporting a first-degree relative with breast cancer increased from 8.1% (95% CI: 7.8, 8.3) to 9.3% (95% CI: 9.0, 9.7), with nearly all of the increase occurring since 2009 (1.1; 95% CI: 0.7, 1.6). The percent reporting a history of a biopsy procedure increased from 26.1% (95% CI: 25.7, 26.5) to 30.1% (95% CI: 30.2, 31.1) between 2000 and 2012. The overall trends suggest that since 2000, the screened population has become more educated and more likely to have markers of higher breast cancer risk. These changes have been most pronounced in recent years, during a period of particularly intense debate regarding screening mammography.

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L12

CANCER INCIDENCE AMONG MINNESOTA TACONITE WORKERS. *Elizabeth M Allen, Bruce H Alexander, Jeffrey H Mandel, Richard F MacLehose, Gurumurthy Ramachandran (University of Minnesota, Minneapolis MN 55455)

Objective: In response to public concerns about health of Minnesota taconite workers, we evaluated cancer incidence in this population. Methods: Through the Minnesota Cancer Surveillance System (MCSS), we identified incident cancers from 1988 through 2010 in a cohort of 41,200 taconite workers born after 1920. Standardized incident ratios (SIRs) were estimated using population base rates from MCSS. Proportion of in-state deaths was used to adjust person-time of the cohort residing in MN, and thus under MCSS surveillance. Smoking habits from a parallel cross-sectional study of current and former taconite workers and Minnesota population based smoking rates from the Minnesota Adult Tobacco Survey were used to estimate a bias factor for smoking. Results: A total of 6,121 incident cancers were identified by MCSS including 931 lung cancers, and 51 mesotheliomas. Crude SIRs for mesothelioma and lung cancer were 1.4 (95% CI: 1.1-1.9) and 0.8 (95% CI: 0.7-0.8) respectively. After adjusting for out-of-state migration, SIRs were 2.4 (95% CI: 1.8-3.2) for mesothelioma and 1.3 (95% CI: 1.2-1.4) for lung cancer. Other elevated cancers include stomach, laryngeal, and bladder. After adjusting with a bias factor for smoking, lung cancer incidence was as expected in MN (SIR = 1.0, 95% CI: 0.9-1.1). Conclusions: Taconite workers have an increased risk for certain cancers. Exposures from taconite operations include crystalline silica, respirable dust and elongated mineral particles. Exposure to commercial asbestos is also possible. Smoking may also contribute to elevated morbidity rates. The extent to which such exposures contribute to disease burden is being further investigated.

L13

PYRETHROID AND ORGANOPHOSPHATE INSECTICIDES & BEHAVIORAL PROBLEMS, CHMS. *Youssef Oulhote, Maryse Bouchard (Université de Montréal, Montreal QC Canada)

Background: Exposure to organophosphate insecticides has been associated with neurobehavioral deficits in children, although data on low levels of exposure experienced by the general population is sparse. Pyrethroids are another class of insecticides rapidly gaining popularity, and epidemiological evidence on their potential effects are lacking. Methods: We used data on 1081 children ages 6 to 11 years from the Canadian Health Measures Survey (2007-2009). We performed logistic regression to examine odds of behavioral problems, indicated by high scores on the Strengths and Difficulties Questionnaire, in relation with pyrethroid and organophosphate insecticides metabolites in urine, adjusting for covariates. Results: Urinary concentrations of organophosphate metabolites were not significantly associated with behavioral problems. Higher concentration of the pyrethroid metabolite cis-DCCA was associated with behavioral problems ($p = 0.03$), and there was a trend for trans-DCCA ($p = 0.12$). For a 10-fold increase in cis-DCCA and trans-DCCA concentrations, the odds ratios (ORs) were 2.0 (CI95%, 1.1 to 3.6) and 1.6 (CI95%, 0.9 to 3.0), respectively. Another metabolite common to many pyrethroids, 3-PBA, was associated with conduct disorders among girls (OR, 2.2 [CI95% 1.0, 4.9]) but not boys (OR, 0.6 [CI95%, 0.3, 1.4]), although this association did not remain significant after accounting for the complex design ($p = 0.10$). Conclusion: We did not observe the previously reported association between organophosphate insecticides and behavioral problems in children. However, our findings suggest that pyrethroids were associated with these problems. This is the first study to suggest this, and further research is needed on potential risks of exposure to pyrethroid insecticides for children's development.

L14

SENSORY IMPAIRMENTS AND COGNITIVE FUNCTION IN THE BEAVER DAM OFFSPRING STUDY. *Karen J Cruickshanks, Carla R Schubert, Mary E Fischer, Guan-Hua Huang, Barbara E.K Klein, Ronald Klein, Dayna S Dalton, Alex Pinto (University of Wisconsin School of Medicine and Public Health, Madison WI 53726)

Background: Age-related sensory dysfunctions may reflect underlying neurological changes in aging and predict risk of cognitive impairment. The association between baseline sensory impairments and cognitive function at follow-up was determined in the Beaver Dam Offspring Study. Methods: The baseline examination (2005-2008) included audiometric testing, the San Diego Odor Identification Test, and Pelli-Robson test of contrast sensitivity. Trail Making Test Part A and B (TMTA and TMTB) were measured at baseline and the 5-yr follow-up (2010-2013). Hearing impairment (HI) was defined as pure-tone average > 25dB (either ear), impaired contrast sensitivity (CS) as <1.55 log triplet (better eye) and olfaction impairment (OI) as identifying < 6 of 8 odorants. Results: Time to complete TMTA and TMTB increased 0.8 and 3.3 seconds, on average, during the follow-up (N = 2281, Mean baseline age =49 yrs). In multivariable models adjusting for age, sex, education, diabetes, atherosclerosis, smoking, head injury and depression, HI, CS, and OI were significantly associated with follow-up cognitive function: TMTA (HI = 1.4 seconds longer, CS= 3.4 seconds longer, and OI = 5.5 seconds longer, $p < 0.05$), TMTB (HI = 9.2 seconds longer, CS = 10.4 seconds longer and OI = 18.1 seconds longer, $p < 0.0001$) and TMTB-TMTA (HI = 7.8 seconds longer, CS= 7.0 seconds longer, and OI = 12.6 seconds longer, $p < 0.001$). Results were similar controlling for baseline test performance, presence of cataract, cataract surgery, and age-related macular degeneration. Conclusions: These results suggest that sensory dysfunctions may be early indicators of declining cognitive function (processing speed and executive function) but these relationships are not unique to a single sensory disorder. Sensorineural disorders and cognitive dysfunction, all of which rely on central neural processing, may share common underlying disease pathways. NIH R01AG021917.

L15

THE EFFECT OF NEIGHBOURHOOD CHARACTERISTICS ON THE RISK OF DEPRESSION IN A COMMUNITY SAMPLE WITH DIABETES. *Genevieve Gariepy, Dominic Comtois, Alexandra Blair, Benoit Thierry, Yan Kestens, Norbert Schmitz (Douglas Institute McGill University, Verdun QC Canada)

Background: Depression is frequent in people with diabetes and can have detrimental effects on disease outcomes. The place where people live is thought to affect mental health above and beyond characteristics of individuals. Neighbourhood environments are particularly relevant to people with diabetes who rely on their local area for resources and support. Aim: To investigate the effects of a range of neighbourhood characteristics on depression in people with diabetes. Methods: We used 5 waves of data from 1,601 participants in the Diabetes Health Study (2008-2012). We assessed depression using the Patient Health Questionnaire. We measured neighbourhood deprivation using census data; density of businesses and services and land-use patterns using geospatial data; and level of greenness using satellite data. We estimated the effect of neighbourhood factors on incidence of depression using survival analysis for discrete-time data, adjusting for time-fixed and time varying confounders. We tested different radius sizes for neighbourhoods to find which was most relevant for our sample (500m, 1000m, 1500m). Results: The 5-year cumulative incidence of depression was 26%. Neighbourhood material deprivation, availability of physical activity services and level of greenness had significant effects on the risk of depression, after adjusting for age and sex. Only availability of physical activity services remained significant after adjusting for socioeconomic and health factors. Other neighbourhood features were not significant. Neighbourhood characteristics closer to home (500m radius) were most relevant to depression. Conclusion: Neighbourhoods which have greater availability of physical activity services are associated with lower risk of depression in people with diabetes. Further research is needed to investigate pathways relating this neighbourhood factor to depression.

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L16

ANTE- AND POSTPARTUM DEPRESSION IN GHANAIAN AND IVORIAN WOMEN AND IMPACT ON FEBRILE ILLNESS IN THEIR OFFSPRING: A PROSPECTIVE, LONGITUDINAL BIRTH-COHORT STUDY. *Stephan Ehrhardt (Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 21205)

In low-income countries perinatal depression is highly prevalent but longitudinal data on its influence on child health are rare. We examined the association between maternal depression and children's febrile illness. 654 mother/child dyads in Ghana and Côte d'Ivoire were enrolled in 2010-2011 in a prospective birth cohort for 2-years of follow up. Mothers were examined for depression using the Patient Health Questionnaire depression module antepartum, 3 and 12 months postpartum. The hazard of febrile illness in children of depressed and non-depressed mothers was estimated using a recurrent event Cox proportional hazards model adjusting for country and socio-economic status. The prevalence of antepartum depression in Côte d'Ivoire and Ghana was 28.3% and 26.3% respectively. The prevalences of depression at 3 and 12 months postpartum were 11.8% and 16.1% (Côte d'Ivoire) and 8.9% and 7.2% (Ghana). The crude and adjusted hazard ratios of febrile illness in children of depressed mothers compared to those of non-depressed mothers were 1.57 (95% confidence interval: 1.20, 2.07) and 1.32 (95% confidence interval: 1.01, 2.07) respectively. We constructed a cumulative depression exposure by categorizing mothers as never or once depressed and two or three times depressed. The crude and adjusted hazard ratio in children of recurrently depressed mothers compared to mothers with fewer episodes was 2.20 (95% confidence interval: 1.51, 3.19) and 1.90 (95% confidence interval: 1.32, 2.75) respectively. Perinatal depression was frequent in both countries and associated with febrile illness in the offspring. Evidence accumulates that the high depression prevalence in sub-Saharan Africa may pose a serious public health threat to women and their offspring.

L17

CROSS-SECTIONAL ASSOCIATIONS OF SELF-REPORTED DEPRESSION AND RACIAL DISCRIMINATION WITH BRAIN TISSUE VOLUMES: THE CARDIA STUDY. *Craig Meyer, Pamela Schreiner, Lenore Launer, Harsha Battapady, Julian Wolfson (University of Minnesota, Minneapolis MN 55455)

Depression and perceived discrimination are common psychological conditions associated with adverse cardiovascular health. Limited data exist as to whether these conditions are associated with physiological changes in brain tissue. The aim of this study was to explore associations of depression and discrimination with structural measures of brain tissue in a population-based biracial cohort. The Coronary Artery Risk Development in Young Adults (CARDIA) study recruited black and white men and women ages 18 to 30 years in 1985; seven follow-up exams have occurred, with depression and racial discrimination measured at the year 25 exam along with structural brain magnetic resonance images (MRI) in a subset of 710 participants. Depression was defined as ≥16 on the CES-Depression Scale and racial discrimination was assessed (any/none) using the Experience of Discrimination Index. The associations between depression and discrimination and total, white (WM) and gray matter (GM) tissue volumes were predicted with linear regression models, and ordinal logistic regression was used to examine depression and discrimination with abnormal WM tissue volume cutpoints of 0, <0.3 and ≥0.3 mL. All models adjusted for standard risk factors and intracranial volume. Associations of total and WM volume were -11.5 and -12.8 mL lower, respectively, among those with both depression and discrimination compared to those with neither. Compared to those with no depression, depression was associated with 48% higher odds of having any WM abnormal volume after adjustment; discrimination was not statistically significant. Overall, our study suggests that common psychological conditions of depression and discrimination are associated with lower normal brain volumes and higher abnormal volumes. These cross-sectional data should be replicated longitudinally to understand temporality and consequences of brain volume differences.

L18

PERCEIVED RACISM IN RELATION TO INCIDENT SARCOIDOSIS IN THE BLACK WOMEN'S HEALTH STUDY. *Yvette Cozier, Jeffrey Berman, Lynn Rosenberg (Slone Epidemiology Center at Boston University, Boston MA 02215)

Sarcoidosis is a multisystemic granulomatous disease of unknown cause that disproportionately affects U.S. black women. Some evidence suggests that chronic stress may influence the incidence. Experiences of racial discrimination may be an important stressor in the lives of black women. We assessed self-reported experiences of racism in relation to incident sarcoidosis in the Black Women's Health Study, a follow-up of U.S. black women aged 21-69 years at entry in 1995. Data on sarcoidosis diagnoses and demographic and behavioral factors were obtained by biennial follow-up questionnaires from 1997 through 2011. Racism scores were created from questions asked in 1997 about the frequency of "everyday" racism (e.g., "people act as if you are not intelligent") (5 questions) and of "lifetime" racism (i.e., unfair treatment on the job, in housing, by police). Experiences of racism were also assessed in 2009. The analytic cohort consisted of 47,845 women who completed the 1997 racism questions and did not have a diagnosis of sarcoidosis prior to 1997. During follow-up through 2011, 343 women reported incident sarcoidosis. Incidence rate ratios (IRR) for sarcoidosis with 95% confidence intervals (95% CI) were estimated using Cox proportional hazards models adjusted for age, education, geographic region, smoking, household income, and body mass index. The IRRs (95% CI) for the highest quartile everyday racism relative to the lowest quartile was 1.22 (0.85-1.73) (P trend = 0.16). The IRR for three positive responses to the lifetime racism questions relative to no positive response was 1.02 (0.69-1.50) (P trend = 0.74). In an analysis confined to women who reported the same levels of racism in both 1997 and 2009, there was no association. These results suggest that racism has little influence on the incidence of sarcoidosis.

E-01

CROWD-SOURCED MAPPING OF SEXUALIZED VIOLENCE IN SYRIA. *Jaclyn Blachman-Forshay, L Wolfe, KC Koenen (Columbia University, New York NY 10032)

Background: The ongoing conflict in Syria began in March 2011 with widespread violence reported throughout the country. Sexualized violence is frequently reported months or years after a conflict, resulting in insufficient crime reporting and a delayed ability to prosecute perpetrators. This project is the first time that sexualized violence in conflict has been reported in real time. Methods: The project utilizes Ushahidi crowd-sourcing technology to map sexualized violence reports. Reports are ascertained through Twitter, email, or direct uploads to the website (women undersiegesyria.crowdmap.com) along with Google and YouTube searches in Arabic and English. Reports are uploaded to the crowdmap website. Crowdmapping enables each report to be geospatially plotted and categorized by victims' demographics, type of violence, perpetrator, and additional consequences. Results: We have analyzed 167 reports: 18% included multiple victims. Females aged 7-46 accounted for 80% of reports and 80% include rape. Twenty-one percent of reports included deaths with signs of sexualized violence, 8% anxiety/depression, and 4% pregnancy from rape. Among male victims aged 11-56, 50% of reports included rape and 74% were tortured by government forces within a detention center. Conclusion: Crowd-sourcing methodology enables sexualized violence in Syria to be tracked in real time. Data can be used to implement immediate interventions for victims as well as to determine whether crowd-sourcing is a valid data collection method to provide evidence for war crime prosecution.

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E-02

THE ROLE OF HEAVY PRECIPITATION EVENTS IN WATERBORNE DISEASE OUTBREAKS IN THE UNITED STATES. *Sumiko Mekaru, Sherri Stuver (Boston University, Boston MA 02115)

In the face of climate change, environmental risk factors for disease outbreaks are increasingly important. While heavy rainfall has reportedly contributed to waterborne disease outbreaks (WBDOs), little epidemiologic research on a broad association between heavy precipitation events (PEs) and WBDOs exists. Study of this association epidemiologically is limited by the poor fit of traditional study designs which evaluate outcomes at the individual level. Here, we present a novel approach to the case-crossover design, treating locations as individuals. "Cases" are locations which have had a WBDO and the exposure of interest is the presence of a heavy PE. For each of 92 locations with a CDC-documented WBDO meeting inclusion criteria (1989-2000), we evaluated NOAA rainfall data for the outbreak year and ten years before and after. We identified PEs exceeding defined rainfall thresholds in 24 or 48 hour periods. Repeated conditional logistic regression analysis performed on Monte Carlo sampled control years (n = 1000) produced a median OR of 0.50 (95% CI 0.25-0.90) for a one-day rainfall exceeding 1.5" in the four weeks preceding the outbreak date. Overall, years with a heavy PE had lower odds of a WBDO than those without a heavy PE, strongly contrasting with the only other broad analysis of US WBDOs and PEs. This study's use of WBDOs after 1970s environmental legislation could suggest that the WBDO-PE relationship is modified by clean water infrastructure. While more research is needed on this specific association, this epidemiologically grounded design provides a framework for exploring environmental risk factors for diseases with important public health implications.

E-03

MARGINAL STRUCTURAL MODELS FOR CONTINUOUS EXPOSURES IN THE LONGITUDINAL SETTING: AN APPLICATION TO REPRODUCTIVE EPIDEMIOLOGY. *Katherine Ahrens (Eunice Kennedy Shriver National Instittute of Child and Human Development, Bethesda MD 20892)

Marginal structural models (MSMs) are an appropriate model choice when adjustment for time-varying confounding affected by prior exposure is necessary. In early applications, MSMs were primarily applied to analytical settings with a dichotomous exposure measured at two points over time. MSMs can also be applied in the setting of continuous exposures measured repeatedly over time; however such examples are limited in the epidemiologic literature. The objective of this analysis is to present an application of MSMs for estimation of etiologic effects in the context of repeatedly measured continuous variables, such as that encountered when reproductive hormones are measured multiple times over the course of the menstrual cycle. These hormones, such as estrogen, follicle stimulating hormone, leptin, luteinizing hormone, and progesterone follow a cyclical pattern, driven by a complex process involving intricate feedback loops and coordinated by the hypothalamic-pituitary-ovarian axis. Given the complex feedback mechanisms traditional regression adjustment is inadequate. Using data from the BioCycle Study, which collected reproductive hormone levels at up to 8 time-points per cycle over up to 2 menstrual cycles from 259 healthy regularly cycling women, we will first describe this feedback process and rationale for utilizing MSMs using directed acyclic graphs (DAGs). We will then demonstrate how to estimate the inverse probability weights for a continuous exposure in the longitudinal setting with a focus on checking the underlying assumptions, evaluating the model fit for both the weights and the final model, and interpretation of the results. We will show how MSMs can be easily implemented in standard software packages, and offer a straightforward approach for making inferences about causal effects in the presence of time-dependent confounding in the longitudinal setting with continuous exposures.

E04

STRATIFIED REGRESSION MODELS FOR CASE-ONLY STUDIES. *Elizabeth Mostofsky, Murray A Mittleman (Harvard School of Public Health, Boston, MA, 02115)

Case-only studies provide a useful approach for examining the impact of transient exposures on acute outcomes. Previously, it has been shown that for studies of a common exposure across individuals, such as environmental air pollution, a time-series study using unconditional poisson will provide identical results to a time-stratified case-crossover study using conditional logistic regression. If each individual can experience different exposure levels, such as behavioral factors, one must conduct a matched analysis of either all prior exposure information (conditional poisson) or a random sample of control times (conditional logistic). In the initial case-crossover design, self-reported history of behavioral exposures was ascertained for a random sample of control times. However, when information on the exact timing of exposure is available for each individual (e.g. registry data on vaccination dates), conditional poisson can be used to include the individual's entire exposure history. This approach, referred to in the literature as the self-controlled case series, can be shown to be identical to the case-crossover when exposure information is available for the entire control period. In this presentation, we will show that compared to conditional logistic regression using a sample of control times, conditional poisson using the total exposure history eliminates the problem of overlap bias and it allows for further adjustment for time and other covariates. Others have proposed that monotonic changes over time in case-only studies can be addressed by incorporating a control group or by using a discrete-time approach. We will show the relationship among these approaches using registry data on psychosocial stressors and the rate of cardiovascular events.

E05

AN EPIDEMIOLOGICAL APPROACH TO THE EFFECTS SUBLUXATION-BASED CHIROPRACTIC CARE HAS ON MANAGING CVD RISK FACTORS: A CASE STUDY AND REVIEW OF THE LITERATURE. N.A Blume, E.L Zielinski (Life University, Marietta GA 30062)

Objective: We present the findings in which a 54 year old male experienced lipid panel normalization as a result of subluxation-based chiropractic care. Clinical Features: 54 year old male first presented into the office with a chief complaint of dyslipidemia. He had a past history of myocardial infarction and angioplasty. One month prior to care patient had a lipid panel drawn indicating that his total cholesterol levels were 124, LDL levels were 63, HDL levels were 38, and triglyceride levels were 116. Other complaints included anxiety, constipation, fatigue, irritability, mood swings, neck pain, and stiff neck. Occupational and personal stress levels were reported 8 out of 10. He also reported depression. Intervention and Outcomes: Paraspinal surface electromyography, range of motion, and thermography readings were taken on the initial visit, on the twelfth visit one month later, and fifteen days after his second blood draw (4 ½ months into care). In conjunction with the above findings, vertebral subluxations were confirmed at the levels of C1, C5, pelvis, and sacrum. Care plan included thirty one patient visits over a five month period before blood draw confirmed that his cholesterol levels decreased. No reportable lifestyle changes occurred beside chiropractic care. In response to the positive blood work results, the patients' cardiologist reduced his medications.Conclusions: We offer a brief historical account of the role cholesterol has played in CVD and provide the most recent global data. Our review reveals that the "cholesterol is harmful" hypothesis is not ubiquitously supported by the literature. There appears to be a growing paradigm shift that subscribes to the theory that psychogenic stress-related inflammatory and hormonal responses are key components to atherosclerotic plaque build-up and subsequent CVD. A review of the chiropractic literature indicates that there is a well-documented relationship between subluxation-based chiropractic care and reduced psychological and physiological stress levels, reduced inflammatory markers, and normalized hormone levels. This suggests that chiropractic care may have a direct impact on lowering primary CVD risk factors. The results of this case study has warranted further research to substantiate these relationships.

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E06

MODELS APPROPRIATE FOR THE STUDY OF PATHOGENS EXHIBITING EXTRA-HOST POPULATION DYNAMICS. *P Ayscue, C Lanzas, YT Grohn. (Cornell University, Ithaca NY)

Mathematical models have been used extensively to study infectious disease dynamics and typically track host characteristics as a proxy for the pathogen under study. These models generally function well in the study of disease transmitted primarily through contact, however, the formulation of a model at the host scale limits the researcher's ability to study salient pathogen-scale dynamics. As a result, host-based models have limited efficacy for the study of pathogens with more complex propagation dynamics, such as foodborne and environmentally transmitted diseases. Here we develop pathogen-scale models based in an ecological metapopulation framework, allowing us to study populations of organisms capable of moving between and growing in spatially segregated habitats. As an informative example, we consider Escherichia coli O157:H7 dynamics in cattle. By applying the above methods, we are able to disaggregate environmental and host contributions to E. coli maintenance in a farm environment and demonstrate that host-based contact is not an important driver in the system, a novel finding. We find that the pathogen-scale framework offers significant improvements over host-scale models for studying diseases with complex population dynamics by intuitively accounting for: extra-host population dynamics, transmission between heterogeneous environments, multiple high-dose challenge events to hosts, environmental stochasticity, quantifying bacterial loads in multiple habitats, and imperfect testing regimens that relate pathogen dynamics to common host-scale observations. The net effect is that researchers are able to examine the contribution of extra-host replication to the overall propagation of the pathogen. We conclude that the ecological metapopulation framework represents an important alternative for epidemiologists for the study of pathogens with substantial extra-host population dynamics.

E07

PARADOXES IN EPIDEMIOLOGIC RESEARCH: ARE THEY ALL JUST SMOKE AND MIRRORS? *J.S Kaufman, H. R Banack (McGill University, Montreal, QC Canada).)

The published medical literature is replete with examples in which authors report a "paradoxical" finding. A recent PUBMED search for "paradox* [ti]" returned 4000 publications from the past 10 years. One example of an apparent paradoxical finding is known as the "obesity paradox". Obesity is associated with a higher mortality risk in the general population, yet confers a survival advantage in certain disease groups. This so-called "obesity paradox" has been reported in a number of cardiovascular and non-cardiovascular disease populations including coronary artery disease, heart failure, stroke, renal disease, COPD, and diabetes. The objective of this presentation is to use data from the US National Health and Nutrition Examination Survey (NHANES) to demonstrate that the apparent "obesity paradox" is the result of a form of selection bias: stratification on a common effect. One of the most common manifestations of selection bias occurs as a result of conditioning on a variable affected by exposure and sharing common causes with the outcome (known as a "collider" in DAG terminology). Conditioning on a collider distorts the association between exposure and outcome among those selected for analysis and produces the spurious association between obesity and mortality. We will use causal diagrams to provide a conceptual framework for the interpretation of the "obesity paradox" and propose appropriate analytic approaches to reduce this bias including deterministic or probabilistic bias analysis using selection proportions and inverse probability weighting.

E08

APPLICATION OF HIERARCHICAL REGRESSION IN AN EPIDEMIOLOGIC STUDY OF CORRELATED EXPOSURES. *K Upson, VL Holt, AJ De Roos (University of Washington, Seattle, WA 98195)

Correlated exposures frequently occur in epidemiologic studies. Estimating multiple exposure effects using maximum likelihood estimation (MLE) may result in unstable coefficients or lack of model convergence, motivating use of separate models for each exposure. However, this practice does not allow for controlling for correlated exposures. We describe the application of Semi-Bayes hierarchical regression (HR) using SAS macro GLIMMIX to simultaneously evaluate multiple exposures. The method uses information about relationships between multiple exposure effects to adjust estimates towards a prior distribution to improve accuracy and precision over MLE. Using data on 93 cases and 198 controls from the Women's Risk of Endometriosis study, we investigated endometriosis risk in relation to correlated urinary phthalate metabolite concentrations using a mixed effects logistic model, combining models from two levels, and compared results to conventional MLE. The first-stage logistic regression model included 8 phthalate metabolites and 3 covariates (conventional analysis). In the second-stage linear regression model, we regressed first-stage model coefficients on prior covariates, grouping phthalate metabolites by parent phthalate diester with expected similar direction and magnitude of effect. We specified a prior variance corresponding to 95% certainty that true residual effect parameters lie in a 10-fold range. Although the appropriateness of our prior distribution is unknown, several HR model effect estimates had lower confidence limit ratios and were more reasonable (e.g., highest vs. lowest quartile, MEHP: OR 0.5, 95% CI: 0.2-1.2; MEHHP: OR 0.8, 95% CI: 0.3-2.1) compared to conventional MLE estimates (MEHP: OR 0.1, 95% CI: 0.03-0.7, MEHHP: OR 0.2, 95% CI: 0.006-5.7). Using multiple levels of information, HR may improve precision and accuracy of estimates over MLE, while adjusting for correlated exposures.

E09

NON-DIFFERENTIAL ERROR IN AGGREGATED MEASURES OF NEIGHBORHOOD CONTEXT. *Stephen J Mooney, Catherine A Richards, Andrew G Rundle (Columbia University - Mailman School of Public Health, New York NY 10032)

Background: Studies of neighborhood health frequently aggregate individual level data to create contextual measures. For example, percent of residents living below the poverty line and median household income are both aggregations of individual-level measurements of household income. These individual-level measures may be error-prone, yet we know of no exploration of the effect of aggregating erroneous individual-level data for use in multilevel health studies. Methods: Using both GEE and mixed models, we modeled the relationship between neighborhood socio-economic status and individual level BMI using survey data from New York City and from simulated datasets. We assessed the effect of non-differential measurement error at the individual level on parameter estimates for resulting aggregated contextual measures. Results: For neighborhood variables aggregated from dichotomous individual-level measures (e.g. % of residents living below the poverty line), non-differential misclassification at the individual level inflates the group-level parameter estimate to 1/(individual-level sensitivity + individual-level specificity - 1) times its true value. For neighborhood variables aggregated from continuous individual-level measures (e.g. median household income), measurement error at the individual level does not cause bias in the neighborhood-level parameter estimate. Discussion: When using contextual measures created through the aggregation of individual level data, the effect of measurement error at the individual level depends on the specification of the contextual variable. Bias away from the null occurs when a non-differentially misclassified dichotomous individual-level measure is aggregated to reflect the proportion of people with that characteristic.

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E10

AUTOMATED VARIABLE SELECTION PROCEDURES TO IDENTIFY STATISTICAL INTERACTION BETWEEN CORRELATED ENVIRONMENTAL EXPOSURES: THE CASE OF PHTHALATE METABOLITES AND BODY MASS INDEX. *Candace Robledo, Julie Stoner, Hélène Carabin, Linda Cowan, Jennifer D Peck (NICHD, Rockville, MD 20892)

Epidemiological studies of the association between a health outcome and urinary concentrations of several correlated environmental chemical metabolites are increasingly common. We propose that multiple linear regression automated variable selection procedures can be practical tools to identify interactions between a large number of correlated environmental chemical exposure values when modeling a continuous health outcome. A series of simulations were conducted to assess the performance of Backward Stepwise/Elimination, Forward Stepwise, Forward Stagewise, Least Angle Regression, and Least Absolute Shrinkage and Selection Operator methods at identifying interactions in linear regression models for pre-pregnancy body mass index (outcome) and a large number of correlated phthalate metabolites and their pairwise interactions as independent factors in settings with small or moderate sample sizes. Measures of performance, including bias, mean squared error, and the true positive and false positive proportions, were calculated for the specified model. Simulations indicated that forward stepwise, modified to adhere to the hierarchical interaction/main effect principle, and unmodified least angle regression performed well (high true positive proportion and low false positive proportion) at identifying interaction among urinary phthalate metabolites. Automated variable selection procedures can efficiently identify a subset of potentially interacting co-exposures that can then be evaluated more thoroughly.

E11

A PROBABILISTIC SENSITIVITY ANALYSIS TO ESTIMATE THE IMPACT OF DATA ERRORS IN A RANDOMIZED TRIAL. *Elisa L Priest, Lori A Fischbach (University of Texas, School of Public Health, Ft Worth TX 77030)

This study quantified the bias from data processing errors on the estimate of effect in a randomized clinical trial of the effectiveness of two different drug regimens on eradication of H. pylori. Data management can impact the frequency of data errors in clinical trials. However, there is little epidemiology literature showing the impact of data errors on the accuracy and precision of the estimates of effect in clinical trials. This study used data from a published randomized clinical trial and a probabilistic sensitivity analysis to correct the raw data for multiple data errors. This produces a simulation interval that reflects the range of potential estimates of effect. The simulation was performed with 10,000 repetitions each for non-differential errors in exposure (treatment), outcome (H. pylori eradication), stratification variable (histology), and all three combined. The original point estimates were compared with the simulation interval to examine the potential bias in the original analysis. The overall results comparing the two treatments showed a bias in the original analysis towards the null. In the simulation with all three errors, the original analysis biased towards the null (Risk Difference 1.5 [-9.7, 12.7]) compared with the mean simulation interval (Risk Difference 1.8 [-11.0, 14.0]). In contrast, when stratified by histologic diagnosis, the original results were biased away from the null in all strata compared with the simulation.This sensitivity analysis showed that nondifferential errors in data processing can bias the risk difference in a randomized clinical trial. Use of sensitivity analysis can correct for multiple biases in study data and show a more complete picture of the study results than a single point estimate.

E12

DATA MANAGEMENT IN EPIDEMIOLOGY STUDIES WITH LIMITED RESOURCES. *Elisa L Priest, Lori A Fischbach (University of Texas, School of Public Health, Ft Worth TX 77030)

The goal of epidemiologic research is to accurately estimate the frequency of disease or the effect of an exposure on the occurrence of disease. This relies on study design, analysis methods, research conduct, handling and processing of the data and the resulting data errors. Two areas that are limited in the epidemiologic literature are project management and data management. Project management can provide epidemiologists with the knowledge, skills, tools, and techniques to manage the scope, quality, schedule, budget, resources, and risk of a research study. Data management includes handling, monitoring, and controlling data as it is collected, processed, combined, and interpreted. Data management processes may impact both the expense of a study and the validity and precision of the estimates of effect in primary and secondary analyses. There are no practical resources to assist epidemiologists with planning and implementing data management processes in a non-regulated study with resource constraints. I created a pragmatic, project-management based, framework that an epidemiologist can use to plan and implement data management. This framework is based on the principles found in the US government regulations for data management in research and is targeted towards those study types commonly encountered by researchers with limited resources: non-FDA regulated studies. The framework has three components: a visual outline of outputs (deliverables), a guide for planning data management, and a comprehensive set of customizable tools for planning and executing data management. Together with the guide, these tools lead an epidemiologist through a standardized, documented approach to planning data management for an epidemiologic study with limited resources.

E13

APPLICATION OF NONLINEAR MIXED MODELS WITH HARMONIC TERMS FOR ANALYZING LONGITUDINAL DATA. *K Schliep, S Mumford, P Albert, E Yeung, A Ye, E Schisterman (NICHD, Rockville, MD 20852)

Many physiological functions follow a cyclical pattern. Epidemiologists researching disease affected by biological rhythms typically conduct studies with repeated measurements. Several flexible models have been proposed for characterizing cyclic patterns but often require uniform measurements or are limited in their ability to study covariate effects. We propose application of a parametric nonlinear mixed model with harmonic terms approach, which allows for irregularly timed measurements, produces minimally biased estimates for small samples, and can be easily implemented in standard software packages. Moreover, in addition to allowing for estimation of differences in the mean effect of a covariate, this approach allows for estimation of differences in the amplitude and phase shift of the cyclical pattern. We present the nonlinear mixed model methodology, including how to model time, choose the number of harmonic terms using penalized likelihood, and how to estimate the effect of covariates on the cyclical pattern using a motivating example: the effect of sweetened soda intake on reproductive hormones in the BioCycle Study (n = 259 women followed for up to 16 time points across 2 menstrual cycles). Women who consumed on average? 1 cup/day of sweetened soda had 13.3% (P = 0.04) higher mean free estradiol levels compared to woman who consumed < 1 cup/day after appropriate adjustment. Example code for running these analyses in R and SAS will be provided. The harmonic model offers a unique approach for studying cyclic patterns with few limitations. This work will help bridge the gap between methodological advancements and practical applications in research settings by providing a real-world example and tools for implementation.

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