



ORIGINAL CONTRIBUTIONS

Body Mass Index and Mortality in a General Population Sample of Men and Women

The Buffalo Health Study

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The objective of this research was to investigate the long-term relation between body mass index (BMI) and mortality from all causes and from specific causes in the general population. A 29-year follow-up study was conducted in a random sample of white men ($n = 611$) and women ($n = 697$) aged 20–96 years who were residents of Buffalo, New York, in 1960. At baseline, height and weight were determined by self-report. BMI was calculated as weight (kg)/height (m^2). During the follow-up period, 295 (48.3 percent) men and 281 (40.3 percent) women died. With the Cox proportional hazards model and adjustment for age, education, and cigarette smoking, a significant linear association was found between BMI and all-cause mortality in men less than age 65 years at baseline (relative risk (RR) = 1.06, 95 percent confidence interval 1.02–1.09), but not in women (RR = 1.02, 95 percent confidence interval 0.99–1.05). In men age 65 years and older, the relation was quadratic in form ($p = 0.02$), with the lowest risks appearing in the BMI range of 23–27. BMI was most strongly related to cardiovascular disease (CVD) and coronary heart disease mortality in women and younger men. No such associations were observed in older men. BMI was not related to an increased risk of death from non-CVD or cancer in either sex. These findings illustrate the importance of BMI as a risk factor for CVD and coronary heart disease mortality in certain gender-age groups and indicate that the majority of the impact of BMI on overall mortality is due to the strong relation between relative weight and these specific causes of death. *Am J Epidemiol* 1997;146:919–31.

body mass index; mortality

Since the early 1960s, Americans have made substantial improvements in the levels of a number of coronary heart disease (CHD) risk factors (1–6). For example, the mean serum cholesterol level in US adults decreased 15 mg/dl from the 1960–1962 National Health and Examination Survey I to the 1988–1992 National Health and Nutrition Examination Survey III (7). The number of Americans who reported better diagnosis and treatment of elevated blood pressure has also increased (2, 3). Finally, lower prevalence rates of cigarette smoking have been reported in

many subgroups of the population, with the one exception being adolescent and young adult females (8). A trend that has not been decreasing and, in fact, appears to be worsening is that Americans have been getting heavier over time (9).

Obesity has been shown to be positively related to a number of CHD risk factors and other health risks (10–17), as well as to mortality (18–26). However, the association between mortality and body weight throughout the range of weight has been described as being J-shaped, U-shaped, inverse, positive, and absent (18–27). The more recent prospective studies, which took into consideration the major limitations of previous research as described by Manson et al. (28), such as failure to control for cigarette smoking, inappropriate control for physiologic effects of disease risk factors, and failure to control for loss of weight due to subclinical disease at baseline, have claimed a significant, direct relation between body weight and overall mortality (25, 26). Evidence also suggests that it may take a substantial period of time for the risks of being

Received for publication January 17, 1997, and in final form July 25, 1997.

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular diseases; MAP, mean arterial blood pressure.

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overweight to become manifest. Results from the Framingham Heart Study indicated that a significant independent relation between relative weight and CHD incidence did not emerge until after 8 years of follow-up in men and 14 years in women (11).

Given that 1) the prevalence of overweight Americans is increasing (9), 2) many recent studies examining body weight and mortality have focused on very select populations (25, 26), and 3) findings from the Framingham Heart Study indicate that a long follow-up may be needed to detect an independent risk of being overweight (11), our goal was to examine the long-term (29-year) relation between relative weight and mortality in a randomly selected sample of the general population. Body mass index (BMI) was utilized as an indicator of relative weight, with all-cause mortality as the primary outcome. Since there is no reason to assume that BMI is related to all diseases to the same degree, the relations between BMI and specific causes of death (cardiovascular diseases, coronary heart disease, noncardiovascular diseases, and cancer) were investigated as well. We also examined the shape of the relation, particularly whether any excess mortality risks existed in individuals with the lowest BMI. Careful consideration was given to reduce possible biases and limitations of previous studies.

MATERIALS AND METHODS

Study population

In 1960, 2,273 men and women aged 15–96 years were enrolled in the Buffalo Blood Pressure Study, an epidemiologic investigation designed to examine factors related to hypertension. The study sample was randomly selected from the general population of Buffalo, New York, using the City Directory as the sampling frame (29). All City of Buffalo census tracts were represented, and 1,369 households were randomly selected, for an overall sampling ratio of 7.7 per thousand. At least one person from a total of 1,082 households agreed to take part in the study, for a participation rate of 79.0 percent (29).

Our study focuses on the follow-up of the 866 white men and 1,050 white women. Excluded from the analyses were 90 (10.4 percent) males and 86 (8.2 percent) females who were less than age 20 years at baseline since there was the likelihood that they were still growing and that their baseline reported height would not be indicative of their adult height, 58 (6.7 percent) males and 71 (6.8 percent) females with insufficient data available for follow-up, and 35 (4.0 percent) males and 48 (4.6 percent) females with incomplete data for BMI and potential covariates. In addition, to

reduce potential bias due to weight loss-related illness, 70 (8.1 percent) men and 70 (6.7 percent) women who reported a physician-diagnosed history of heart disease, stroke, cancer, or diabetes mellitus at baseline were excluded. Two (0.2 percent) males and 78 (7.4 percent) females were excluded as lost-to-follow up. These exclusions resulted in a total of 611 white men and 697 white women aged 20–96 years and free of known disease at baseline available for inclusion in the analysis. Black men ($n = 155$), black women ($n = 190$), and other minority groups ($n = 12$) were not included at this time because of incomplete follow-up in these race-gender groups.

Follow-up of the cohort and ascertainment of vital status

A prospective study design was utilized, and the average length of follow-up was 29 years, beginning with each participant's baseline date of interview (June 1960 through December 1961) and ending on December 31, 1989. Vital status was determined, and participants were followed until their death or until the termination of the study.

Procedures to locate the cohort members were initiated in 1990 and were completed over the subsequent 5 years. Vital status was determined by using computerized searches of the New York State Department of Health Vital Records Death Registry, the Cancer Tumor Registry, the Department of Motor Vehicles records of drivers' licenses and automobile registrations, and the United States Social Security Administration Death Master Files. Manual searches of the telephone and Polk directories for the City of Buffalo and surrounding suburbs were also conducted. Other methods of follow-up included contacting the individual's last employer (as of 1960), church, or other organizations listed on the original questionnaire. Polk and telephone directories were also utilized to locate neighbors, who were telephoned to obtain information regarding the current location of study participants.

Vital status of living participants was confirmed by telephone or mail correspondence with the participant, a direct family member, or other acquaintance (i.e., nursing home worker). Death certificate data were utilized with rigid matching criteria (exact spelling of last name and exact date of birth) to determine participant deaths. Match results were manually reviewed on an individual basis.

Outcome measures

The study outcomes were mortality from all causes and from specific causes, including cardiovascular diseases (CVD), CHD, all noncardiovascular diseases

(non-CVD), and cancer. For all deaths, the date and underlying cause of death noted on the death certificate were used to ascertain time and cause of death. *International Classification of Diseases* codes were upgraded to the ninth revision by a trained nosologist. All deaths that occurred in the study population between the baseline interview and December 1989 were considered in the analysis for all-cause mortality. The following *International Classification of Diseases*, Ninth Revision, codes were utilized to classify the specific causes of death: 390–459, CVD; 410–414, CHD; all codes except 390–459, non-CVD deaths; and 140–209, cancer.

Baseline measures

At baseline, a 70-item questionnaire was administered by the interviewer in each participant's home to obtain information regarding anthropometric, social, and lifestyle variables. Systolic and diastolic blood pressures were measured three times throughout the interview in each individual in a standardized manner by trained personnel using a standard mercury sphygmomanometer. Measurement was made to the nearest 2-mm scale indicator. Systolic pressure was recorded as the first phase (level of first audible sound). Diastolic pressure was recorded as the fifth phase (level of absence of sound). The blood pressure index utilized in our study was the mean arterial blood pressure (MAP), calculated as the diastolic pressure (DBP) plus one third of the difference between systolic (SBP) and diastolic pressures ($MAP = DBP + 1/3(SBP - DBP)$). The mean of the second and third blood pressure measurements was used in the above calculation. Height and weight were determined by self-report. Other information obtained by self-report included age (in years), cigarette smoking history (in packs/day), education, and medical history. Detailed information was gathered on usual physical activities performed during work and leisure time. A physical activity index indicative of participants' total weekly energy expenditure (kcal/kg/hour) was calculated as recommended by Ainsworth et al. (30).

Body mass index was calculated as body weight (kg)/height (m^2). A cutpoint of 27.50 for men and 27.13 for women was utilized to characterize participant's weight status. These values represent the fourth quartile of the BMI distribution in both sexes and approximately represent the 85th percentile of BMI for white males and females aged 20–29 years from the National Health and Nutrition Examination Survey I (31). This decision was based on recommendations by Must et al. (31), suggesting that from a public health standpoint it may be most prudent to classify adult

overweight status on the basis of young adult standards.

Statistical analysis

Cox proportional hazards model (32) was utilized to examine the relations between BMI and mortality from all causes and from specific causes and to test for potential interactions between BMI and various covariates. Body mass index was utilized as a continuous variable. In all analyses aimed at describing the shape of the BMI-mortality associations, we categorized BMI into sex-specific quartiles and used the lightest quartile as the reference group. Age and education (in years) and cigarette smoking (in packs/day) were considered as continuous covariates. These variables were selected on the basis of their known relation to both BMI and mortality. Separate models that included mean arterial blood pressure were tested to enable us to ascertain the contribution of MAP to the BMI-mortality relations. Additional analyses were performed, adjusting for participants' physical activity levels.

To test for nonlinear quadratic trends for both all-cause mortality and CHD mortality, we used statistical models that included both quadratic and linear terms for BMI entered as a continuous variable. All analyses were repeated, excluding individuals who died within the first 5 years of the study to rule out the possibility that unknown underlying disease at baseline may have resulted in weight loss and influenced early mortality.

To explore the relation between overweight status and all-cause mortality throughout the 29 years of the study, we plotted cumulative survival curves at the mean of age, education, and packs of cigarettes smoked comparing individuals above and below the previously described BMI cutpoints, starting at baseline and continuing through the end of the follow-up period.

The validity of the underlying assumption of the Cox model, that the proportional hazard does not change with time, was tested for each outcome studied, with age, education, and cigarette smoking included in the model as covariates. No evidence of violation of this assumption was found in males or females. Statistical Package for the Social Sciences for Windows (33) was utilized to conduct the Cox proportional hazards survival analyses and to examine the relation between categories of weight status over the 29 years of follow-up. Statistical significance was declared when a two-tailed *p* value of less than 0.05 was observed. Ninety-five percent confidence intervals were calculated around point estimates of risk.

RESULTS

In males, statistical testing for potential interactions revealed a significant interaction between BMI and age when age was utilized as a dichotomous variable (<65 vs. ≥65 years) and mortality from all causes, CHD, and CVD were the outcome measures. Age 65 years was chosen since it represents a commonly used cutpoint for identification of elderly subjects. Preliminary analyses indicated that this cutpoint appropriately defined the interaction. No meaningful BMI × age interactions were observed in females for any outcome studied. The baseline characteristics of the study participants are presented separately for males and females across the entire age range and stratified by age (table 1).

The mean weight for men was 78.2 (12.2) kg, and the men were 1.75 (0.07) m tall, with a mean BMI of 25.5 (3.6) kg/m². The average weight for women was 64.7 (12.5) kg, they were 1.62 (0.07) m tall, and they had a mean BMI of 24.7 (4.7). Mean age at baseline was 45.8 (5.6) years for men and 45.5 (15.8) years for women, while the average number of years of education was 10.5 (3.5) and 10.2 (3.0) for men and women, respectively. Nearly 75 percent of the men smoked cigarettes, for an average of 1.3 packs/day, including

nonsmokers. Fewer women (53.2 percent) reported smoking cigarettes, and they averaged less than one pack/day.

In males, those aged 65 years and older weighed less, were shorter and less educated, and had higher systolic pressures than did their younger counterparts. The older men also smoked fewer cigarettes per day and were less physically active than were those under age 65 years. BMI did not differ between the age groups. Older women weighed more, were similar in height, and, consequently, had higher BMI levels than did younger women. As with the men, older women had fewer years of education and smoked less compared with women younger than age 65 years. No differences between the age groups were apparent for physical activity, but systolic and diastolic pressures were higher in older compared with younger women.

During the 29-year follow-up period, 295 (48.3 percent) men and 281 (40.3 percent) women died (table 2). As expected, CVD deaths represented the leading cause of death in both genders and age groups, with a total of 154 (25.2 percent) men and 153 (22.0 percent) women dying from CVD. CHD deaths accounted for the largest portion of the CVD deaths (70.1 percent in men and 53.6 percent in women). Sixty-nine (11.3

TABLE 1. Characteristics of the Buffalo Health Study participants at baseline, 1960

Characteristics	Age group (mean (standard deviation))		
	Entire sample	Ages 15–64 years	Ages 65–96 years
<i>Men</i>			
No.	611	518	93
Weight (kg)	78.2 (12.2)	78.7 (12.2)	75.0 (11.5)*
Height (m)	1.75 (0.07)	1.75 (0.07)	1.72 (0.07)**
Body mass index (kg/m ²)	25.5 (3.6)	25.6 (3.6)	25.3 (3.7)
Age (years)	45.8 (5.6)	41.3 (12.0)	71.2 (6.7)**
Education (years)	10.5 (3.5)	11.0 (3.3)	8.1 (4.0)**
Cigarettes smoked (packs/day)†	1.3 (0.9)	1.4 (0.9)	0.9 (1.01)**
Systolic blood pressure (mmHg)	142.5 (22.5)	139.8 (21.1)	157.5 (24.7)**
Diastolic blood pressure (mmHg)	88.0 (13.8)	87.7 (13.8)	89.9 (3.7)
Mean arterial pressure (mmHg)	106.2 (15.4)	105.1 (15.2)	112.5 (15.5)**
Physical activity (kcal/kg/hour)	1.9 (0.4)	1.9 (0.4)	1.6 (0.3)**
<i>Women</i>			
No.	697	600	97
Weight (kg)	64.7 (12.5)	64.2 (12.7)	67.9 (11.3)*
Height (m)	1.62 (0.07)	1.62 (0.06)	1.62 (0.08)
Body mass index (kg/m ²)	24.7 (4.7)	24.5 (4.7)	26.3 (4.9)*
Age (years)	45.5 (15.8)	41.3 (12.5)	71.6 (5.8)**
Education (years)	10.2 (3.0)	10.6 (2.8)	7.9 (3.4)**
Cigarettes smoked (packs/day)†	0.7 (0.80)	0.8 (0.8)	0.3 (0.6)**
Systolic blood pressure (mmHg)	138.2 (27.4)	133.6 (24.7)	166.6 (26.5)**
Diastolic blood pressure (mmHg)	83.7 (15.0)	82.5 (14.6)	91.4 (15.2)**
Mean arterial pressure (mmHg)	101.9 (18.1)	99.5 (17.1)	116.5 (17.3)**
Physical activity (kcal/kg/hour)	1.7 (3.0)	1.8 (0.7)	1.9 (1.3)

* $p < 0.01$; ** $p < 0.001$, gender-specific t tests for age group differences.

† Includes nonsmokers (25.5% of men and 48.8% of women).

TABLE 2. Vital status and cause of death in deceased participants of the Buffalo Health Study as of December 31, 1989

	Entire sample		Age group			
			Ages 15-64 years		Ages 65-96 years	
	No.	%	No.	%	No.	%
<i>Men</i>						
Vital status						
Alive	316	51.7	314	60.6	2	2.2
Deceased	295	48.3	204	39.4	91	97.8
Cause of death						
Cardiovascular diseases	154	25.2	96	18.5	58	62.4
Coronary heart disease	108	17.7	66	12.7	42	45.2
Cancer	69	11.3	49	9.5	20	21.5
Respiratory disease	28	4.6	22	4.2	6	6.5
Injury	5	0.8	5	1.0	0	0.0
Noncardiovascular diseases	141	23.1	108	20.8	33	35.5
Total no.	611	100.0	518	84.8	93	15.2
<i>Women</i>						
Vital status						
Alive	416	59.7	414	69.0	2	2.1
Deceased	281	40.3	186	31.0	95	97.9
Cause of death						
Cardiovascular diseases	153	22.0	89	14.8	64	66.0
Coronary heart disease	82	11.8	51	8.5	31	32.0
Cancer	68	9.8	52	8.7	16	16.5
Respiratory disease	12	1.7	7	1.2	5	5.2
Injury	7	1.0	4	0.7	1	1.0
Noncardiovascular diseases	128	18.4	97	16.2	30	30.9
Total no.	697	100.0	600	86.1	97	13.9

percent) cancer deaths were recorded in men and 68 (9.8 percent) in women.

Using Cox proportional hazards survival analyses, we examined the nature of the relation between BMI and mortality from all causes and specific causes over time in men and women separately and by age groups in men when necessary due to significant age \times BMI interactions. In men less than age 65 years, the quadratic BMI term was determined to be nonsignificant for all-cause, CVD, and CHD mortality. Among the older men, this was not the case. The quadratic BMI term was significant for all-cause ($p = 0.02$) and CHD ($p = 0.047$) mortality, and it approached significance for CVD ($p = 0.09$) deaths. For cancer and non-CVD mortality, no significant quadratic relations were found when men of all ages were studied together. In women, the quadratic term for BMI was nonsignificant for mortality from all causes, CVD, and CHD, while for non-CVD and cancer mortality, the significance levels were both $p < 0.01$.

The results of the Cox proportional hazards survival analyses, using BMI as a continuous variable with

mortality from all causes and specific causes as the outcomes, are presented in table 3 for men and women separately. Results are shown only for age-gender groups in which no significant interactions or quadratic BMI terms were found. In the younger men, BMI at baseline was associated with a statistically significant 6 percent increased age-, education-, and smoking-adjusted risk of death from all-cause mortality. The influence of BMI on CVD and CHD mortality was somewhat greater than that observed for overall mortality, with a significant multivariate-adjusted relative risk of 1.10 (95 percent confidence interval (CI) 1.06-1.15) noted for CVD mortality and 1.12 (95 percent CI 1.07-1.18) for CHD mortality. As expected, the addition of MAP to the models resulted in a slight attenuation of the relative risks. BMI was not associated with risk of death from non-CVD or cancer in men aged 15-96 years.

Among women, the only significant association observed was between BMI and CHD mortality (age-, education-, and smoking-adjusted relative risk = 1.06, 95 percent CI 1.01-1.11). When MAP was included in

TABLE 3. Relative risks of death from all causes and specific causes according to baseline levels of body mass index as a continuous variable, the Buffalo Health Study, 1960–1989

	All men (n = 611)		Men aged <65 years (n = 518)		Women (n = 697)	
	Relative risk	95% confidence interval	Relative risk	95% confidence interval	Relative risk	95% confidence interval
<i>All-cause mortality</i>						
Age-adjusted relative risk			1.04	1.01–1.08	1.01	0.99–1.04
Multivariate relative risk*			1.06	1.02–1.09	1.02	0.99–1.05
Multivariate relative risk†			1.04	1.00–1.08	1.01	0.98–1.04
<i>Specific cause mortality</i>						
<i>Cardiovascular disease</i>						
Age-adjusted relative risk			1.08	1.04–1.13	1.03	0.99–1.06
Multivariate relative risk*			1.10	1.06–1.15	1.02	0.98–1.06
Multivariate relative risk†			1.08	1.03–1.13	1.00	0.96–1.04
<i>Coronary heart disease</i>						
Age-adjusted relative risk			1.11	1.06–1.16	1.05	1.01–1.10
Multivariate relative risk*			1.12	1.07–1.18	1.06	1.01–1.11
Multivariate relative risk†			1.10	1.05–1.16	1.04	0.98–1.09
<i>Noncardiovascular diseases</i>						
Age-adjusted relative risk	1.00	0.95–1.05				
Multivariate relative risk*	1.00	0.95–1.05				
Multivariate relative risk†	1.00	0.95–1.05				
<i>Cancer</i>						
Age-adjusted relative risk	0.96	0.89–1.03				
Multivariate relative risk*	0.95	0.88–1.02				
Multivariate relative risk†	0.96	0.89–1.04				

* Adjusted for age (years), education (years), and cigarette smoking (packs/day).

† Adjusted for age (years), education (years), cigarette smoking (packs/day), and mean arterial blood pressure (mmHg).

the analyses, the relative risk was reduced to 1.04 and was no longer statistically significant. For all-cause mortality and CVD mortality, all age- and multivariate-adjusted relative risks were above one, but the confidence intervals each included one.

Figures 1 and 2 illustrate the results of analyses for overall and cause-specific mortality endpoints classifying male and female participants, respectively, into gender-specific quartiles of BMI. For men (figure 1), all-cause, CVD, and CHD mortality results are presented stratified by age group (<65 vs. ≥65 years). In younger men, an increased risk of death from all causes became apparent at a BMI level above 23.0 (quartile 2). In each successive BMI quartile, the risk estimates increased, with men in the highest BMI quartile (BMI ≥ 27.50) experiencing a significant 67 percent increased risk of overall mortality. CVD and CHD mortality were strongly related to BMI in this group of men. The age-, education-, and smoking-adjusted relative risks of CVD mortality in the third and fourth BMI quartiles were 2.77 and 2.96, respectively. Similarly adjusted relative risks for CHD mor-

tality were 2.28 and 3.45. In contrast, in men aged 65 years and older, a BMI in the range of 25.2–27.4 (quartile 3) appeared to be associated with the lowest risk of mortality from all causes, CVD, and CHD, although the results did not reach statistical significance.

No associations were apparent for non-CVD or cancer deaths in the entire cohort of men. Although the point estimates of risk for these causes of death in the two highest BMI quartiles were below one, the 95 percent confidence intervals included unity.

For women (figure 2), the associations between BMI and mortality from CVD and CHD appear to be linear, and in the case of CHD mortality, were about the same magnitude as those observed in men younger than aged 65 years. Women with a BMI above 27.13 (quartile 4) had a significant, nearly 2.6-fold increased risk of dying from CHD compared with women whose BMI was below 21.44 (quartile 1). With regard to the significant quadratic relation between BMI and non-CVD or cancer mortality, no evidence of an increased risk was observed with increasing levels of BMI. For

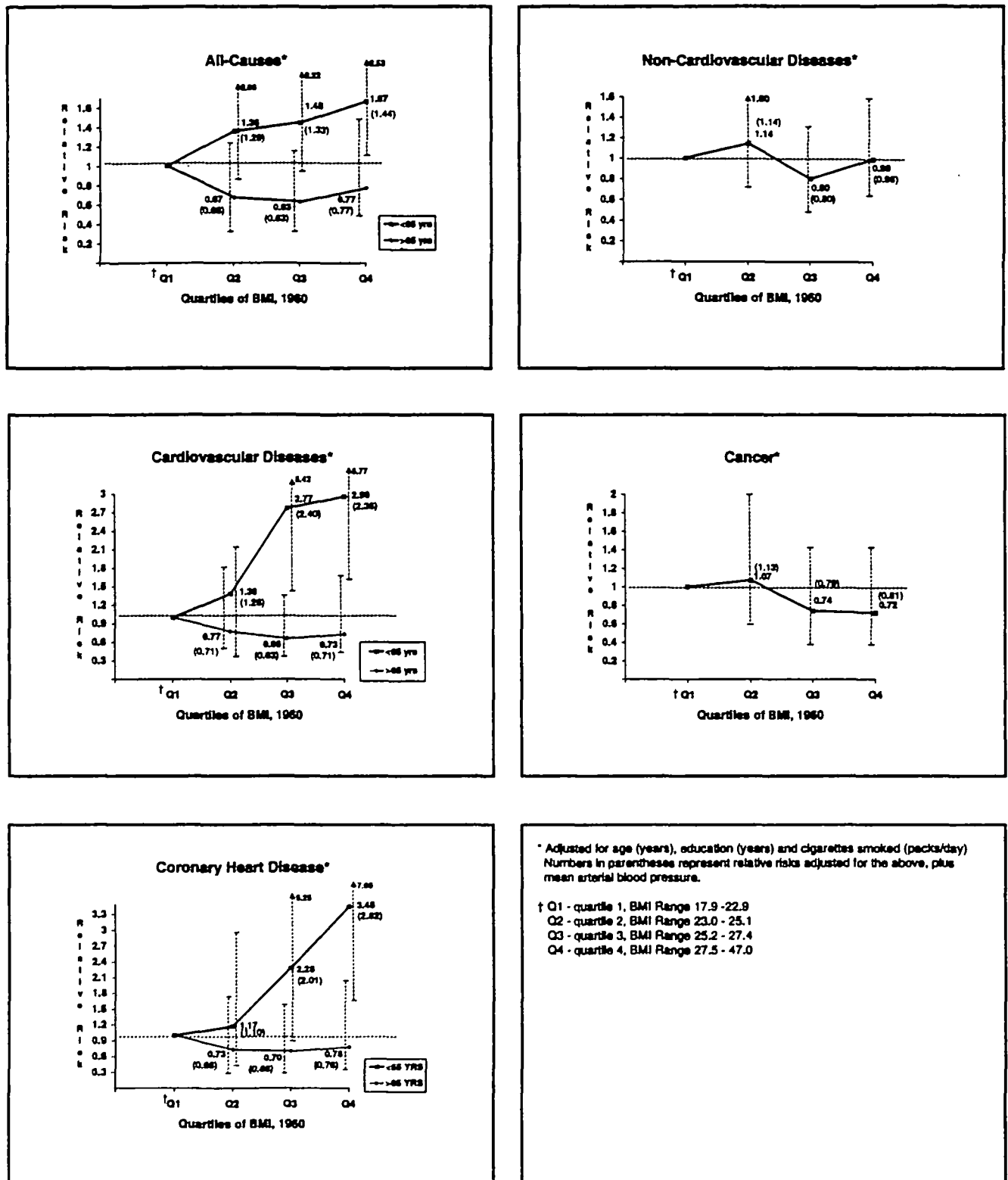


FIGURE 1. Relative risk of all-cause and specific-cause mortality by quartiles of body mass index (BMI) in white males aged 20–96 years ($n = 611$), the Buffalo Health Study, 1960–1989. Analyses for all-cause, CVD, and CHD mortality are stratified by age group (<65 vs. ≥65 years). Analyses are adjusted for age (in years), education (in years), and cigarettes smoked (in packs/day). Numbers in parentheses represent relative risks adjusted for age, education, and cigarettes smoked plus mean arterial blood pressure (in mmHg). The lowest quartile is the reference group. Ninety-five percent confidence intervals are indicated by the vertical bars.

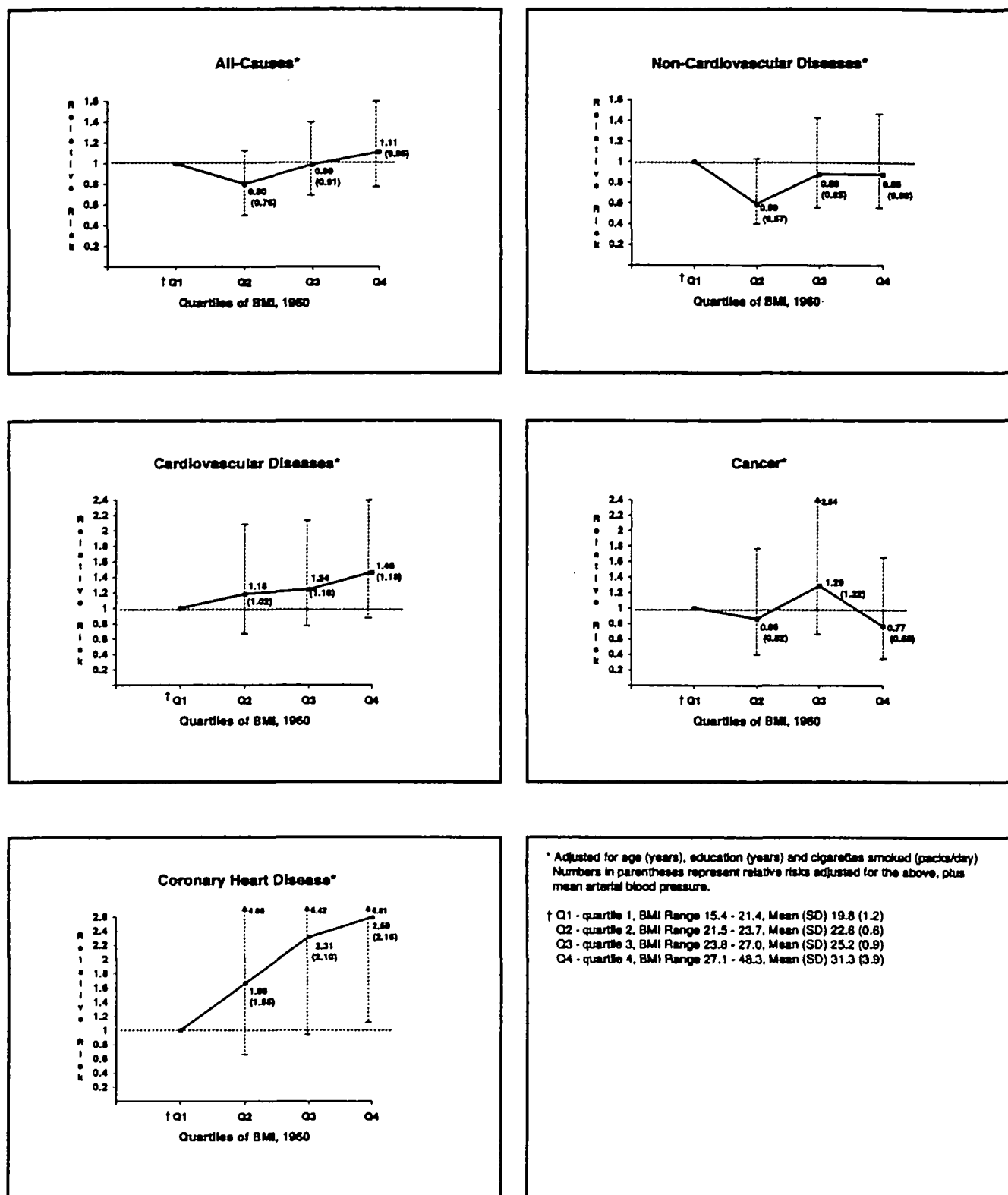


FIGURE 2. Relative risk of all-cause and specific-cause mortality by quartiles of body mass index (BMI) in white females aged 20–96 years ($n = 697$), the Buffalo Health Study, 1960–1989. Analyses are adjusted for age (in years), education (in years), and cigarettes smoked (in packs/day). Numbers in parentheses represent relative risks adjusted for age, education, and cigarettes smoked plus mean arterial blood pressure (in mmHg). The lowest quartile is the reference group. Ninety-five percent confidence intervals are indicated by the vertical bars.

non-CVD mortality, the lowest risk was observed in women with a BMI between 21.5 and 23.7 (quartile 2).

In both sexes, a slight attenuating effect of blood pressure on the BMI-mortality relations was observed mainly for all-cause, CVD, and CHD mortality with little or no effects on non-CVD or cancer mortality. In men, the impact was more apparent in younger compared with older men. In women, the strongest contribution of blood pressure appeared to be on CHD mortality, particularly in nonsmoking women (figure 3).

In women and younger men, results were generally similar when participants who died within the first 5 years after the initial interview were excluded from the analysis. In older men, there was a slight shift, with the lowest all-cause, CVD, and CHD mortality risks now appearing in the second rather than the third BMI quartile. Additional adjustment for the effects of usual work and leisure-time physical activity did not change any of the observed associations in women or in men.

Of the 697 women in the cohort, 326 (46.8 percent) were never-smokers. Recognizing the constraints of the reduced sample size, we repeated the survival analyses in this group of women. The results are illustrated in figure 3. Even among never-smoking women, there was no relation between BMI and all-cause mortality. The survival curves in this group resembled those of the entire cohort; however, the strong BMI-CHD mortality relation was even stronger in never-smokers. Women in the heaviest group, 27 (24.8 percent) of whom died from CHD, experienced an approximate eightfold significant increased risk of CHD death. Too few men ($n = 67$) reported never smoking to permit such analyses in this gender group.

We next examined cumulative survival curves to quantify the length of time needed to observe an impact of increased body weight on all-cause mortality. For these analyses, separate curves were plotted comparing individuals above and below the gender-specific fourth quartile of BMI. For men, the BMI cutpoint was 27.50, and for women, BMI was divided at the level of 27.13. In men, the survival curves were similar until approximately 25 months and then diverged as the follow-up period was extended, indicating that the mortality risk associated with a BMI at or above 27.50 increased over time. In women, differences in the all-cause survival curves did not appear until approximately 100 months (8.3 years) after the baseline interview, and the difference between the two groups stayed fairly constant over time.

DISCUSSION

In our general population sample of white men and women, BMI emerged as an important, independent risk factor for overall mortality in men less than age 65

years, but not in older men. BMI was not related to all-cause mortality in women, even when analyses were restricted to women who reported never smoking cigarettes. In younger male members of the cohort, the relation was linear, with no increased risks noted in individuals with BMI levels below the twenty-fifth percentile. In the older men, this was not the case. The relation was quadratic in form, and the lowest risk was seen in the third BMI quartile.

Previous studies examining the relation between relative weight and all-cause mortality have presented varied findings with regard to the shape of the relation (18–27). The inconsistencies have been attributed to overadjustment of potential biologic mechanisms, failure to properly take cigarette smoking into account, and lack of exclusion of individuals with weight loss-related illness (28). The latter is particularly important in the elderly (34), for whom low body weight is often presumed to be a risk factor for early death. The Buffalo Health Study results for younger men are similar to those reported by others, particularly those who restricted their analyses to former or never-smokers, removed biases due to illness-related weight loss, and did not overcontrol for potential biologic mechanisms (22, 25). We excluded all persons with known disease at baseline and provided separate analyses with and without adjustment for blood pressure, a potential mechanism whereby increased weight may effect mortality. Our primary analyses included adjustment for cigarette smoking, but sample size restrictions, particularly in men, limited our ability to examine the BMI-mortality relations in never-smokers.

The fact that we did not find an increased risk at the low end of BMI in these younger men, despite the fact that current smokers were included, differs somewhat from the findings of others (23, 25). The most plausible explanation for the differences may be the lack of a sufficient number of men with very low BMI levels in our cohort. The BMI range of our lowest quartile was between 17.9 and 23.0, with a mean of 21.5 ± 1.2 , but only four men under age 65 years had a BMI level below 19.0. Therefore, our ability to detect any possible increased risk of mortality in the very lean was limited.

Another potential explanation may be that our follow-up period was 29 years long, and any effects of pre-clinical illness on baseline BMI or early mortality were overridden by the long follow-up. Evidence to this point was provided by the Harvard Alumni Study (25), in which different follow-up periods were examined separately. Within the first 10 years of follow-up, a U-shaped curve was reported. Subsequent follow-up periods revealed first a J-shaped relation and then a linear trend in the last 6 years of follow-up (25).

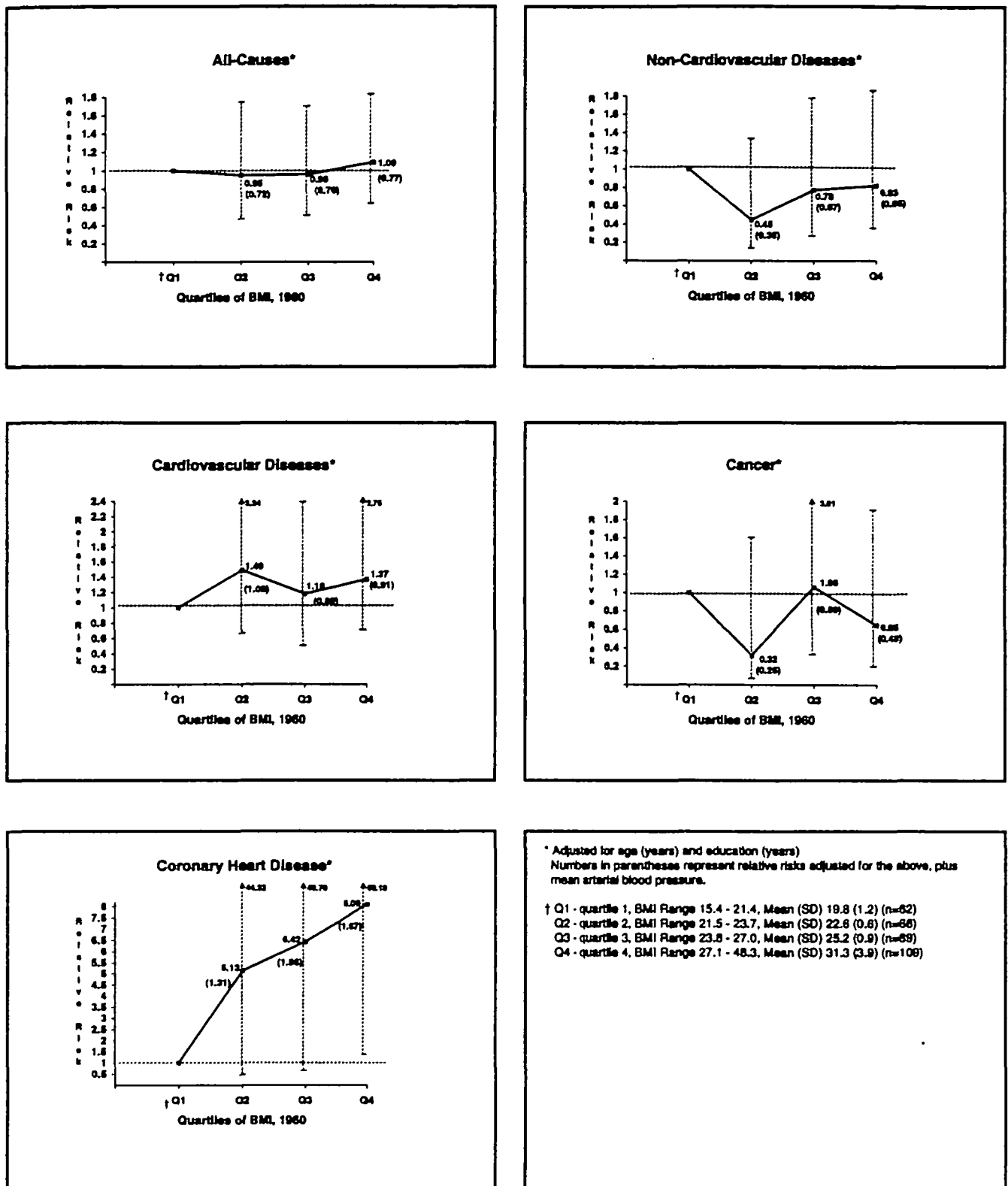


FIGURE 3. Relative risk of all-cause and specific-cause mortality by quartiles of body mass index (BMI) in white females aged 20–96 years who reported themselves as never-smokers at baseline ($n = 326$), the Buffalo Health Study, 1960–1989. Analyses are adjusted for age (in years) and education (in years). Numbers in parentheses represent relative risks adjusted for age and education plus mean arterial blood pressure (in mmHg). The lowest quartile is the reference group. Ninety-five percent confidence intervals are indicated by the vertical bars.

Finally, differences in various study populations may also account for the discrepant findings. Our study population was a randomly selected sample of residents of Buffalo, New York, and likely differs from select populations such as the Harvard Alumni in important health-related characteristics, such as educational attainment and socioeconomic status. In such diverse groups, BMI may have very different socio-demographic and psychosocial correlates and, therefore, different interpretations with regard to mortality.

In men in the older age group, the relations between BMI and mortality from all causes, CVD, and CHD differed considerably from those in younger men. Compared with the first quartile of BMI, estimates of relative risks for all subsequent quartiles were below one, although all confidence intervals included one. For each outcome, the lowest risk estimates were found in the third quartile. Analyses eliminating deaths that occurred in the first 5 years of follow-up had little effect on the results, except that the lowest risks shifted from the third to the second BMI quartile. The lack of data on recent weight loss as well as sample size and statistical power considerations warrant careful interpretation of the results in this age group. However, the possibility that a BMI between 23 and 25 in elderly men may be more advantageous than a lower level cannot be ruled out.

In female members of the Buffalo Health Study cohort, we found no relation between BMI and overall mortality. Our findings corroborate those of others who have reported the lack of an association between BMI and all-cause mortality in women (20, 23, 24) and cannot be attributed to residual confounding due to cigarette smoking, overcontrol for potential mechanisms, or lack of elimination of women with baseline illness, since we took each of these factors into careful consideration.

Of the specific causes of death studied, BMI was most strongly related to CVD and CHD mortality in both sexes. These findings concur with those of others who found CHD or CVD in general to be the specific causes of death most strongly associated with increased relative weight (19, 22, 25, 26). In the Buffalo Health Study women, BMI appeared to be at least as strong a risk factor for CHD as in the younger men. Although the relative risks did not reach statistical significance until BMI was above 27.13 (quartile 4), a positive trend was apparent even in women with an average BMI of 22.6 compared with women in the lowest quartile. Owing to the large number of men who reported smoking at baseline (74.5 percent), we were unable to examine the BMI-CHD mortality relations in never-smokers. However, statistical tests for an interaction between BMI and cigarette smoking

habits were nonsignificant, indicating no differences in the relation between BMI and mortality in smokers compared with nonsmokers. In women who reported never smoking, relative risks at each quartile were greater than those observed in the total cohort of women.

BMI was not associated with non-CVD or cancer mortality in men, while a significant quadratic relation for these outcomes was found in women. Since our cancer endpoint includes a variety of cancer sites and non-CVD deaths include all cancers as well as a mixture of very different causes of death, these findings are not unexpected. The findings in men may partially reflect competing risks of mortality due to the increased risks of CVD/CHD mortality associated with an elevated BMI or may, in fact, be indicative of a lower risk of death from cancer in the heavier men. Therefore, the observed associations for all-cause mortality are predominantly influenced by deaths due to CHD. The relatively small percentage of deaths due to CHD in women (29.2 percent) may be one reason why we found no significant relation between BMI and all-cause mortality in women.

We did not find a strong attenuating effect of blood pressure on any outcome, except perhaps for CHD mortality in nonsmoking women. The implications of this finding are that there are mechanisms other than blood pressure in the causal pathway. It is also possible that secular trends in blood pressure treatment and control are responsible for the small contribution of blood pressure we observed on the BMI-mortality relations.

A major strength of our study is that the participants were a randomly selected sample of the general population of Buffalo, New York, with a baseline participation rate of 79 percent and an average follow-up rate of 93.1 percent. Although the sample size is relatively small compared with other populations studied, this study is unique because it allows comparisons between men and women across a wide age range regarding the long-term relation between BMI and mortality from all causes, as well as from a number of specific causes of death. In addition to supporting research utilizing select populations, our findings provide evidence that the risk of CHD with increasing BMI is generalizable to the general population of white Americans from northeastern industrial cities.

Another strength is the length of the follow-up period. In addition to allowing examination of the long-term relation between BMI and mortality, the 29-year follow-up was long enough that any effects of weight loss early in the study due to subclinical disease at baseline would not influence the overall results. The

long follow-up and the wide range of ages also allow for interesting comparisons by age.

While it is common practice to control for BMI when the association between physical activity and mortality is being investigated, few studies have examined the relations between relative weight and mortality after taking into consideration participants' activity levels. A final strength of our study includes the comprehensive data available regarding physical activity. Addition of this information to the model enabled us to conclude that the observed BMI-mortality relations were independent of any effects of energy expenditure.

One limitation of our study was that height and weight were determined by self-report. Self-reported height and weight may have resulted in an underestimation of BMI, since people tend to overreport their height and underreport their weight (35, 36). However, these errors in estimation tend to be small (35, 36), and our highest quartiles in both sexes closely approximate the 85th percentile of BMI for whites aged 20–29 years, a somewhat conservative cutpoint for overweight status. With these conservative cutpoints, the heaviest women and younger men were at significantly greater risks of death from CHD when compared with their leanest counterparts.

Another potential limitation is that BMI and other characteristics were determined only at baseline, and participants could have changed their body weight and other lifestyle factors (i.e., cigarette smoking) during the follow-up period. Therefore, we were unable to examine effects of changes in weight or weight cycling on mortality. While it is possible that some participants lost weight, traditionally, as Americans age, body weight tends to increase (31, 37). This fact has been accepted by many in the past and is reflected in existing health guidelines that allow for increases in weight with increasing age (38). One exception may be the elderly, in whom weight may have remained relatively stable or even decreased in those who survived to the eldest ages. This measurement bias may have been reflected in the lower point estimates of risk that we observed in this age group.

Finally, no measures of body composition or fat distribution were available from the baseline interview. Therefore, we were unable to examine specific hypotheses regarding the role of body fat or the location of such fat on mortality. It is possible, particularly in men, that a high BMI indicates muscularity rather than adiposity. Given that our population is a random sample of residents of Buffalo, New York, it is unlikely that a large percentage of individuals with high BMI levels are particularly muscular. Fat distribution, measured by the waist-to-hip circumference, was

found to be a better predictor of mortality in woman than was BMI (39), and measures of fat distribution may have provided important information to help explain any observed mortality differences between men and women. Nevertheless, height and weight are relatively easy to measure in a clinical setting, and our study results concur with others that show that being overweight is related to higher mortality risks, especially from CHD (22, 25, 26).

In conclusion, our findings provide yet another piece of evidence illustrating the importance of BMI as a risk factor for CHD mortality in men and women. This increased risk contributes to a significant increased risk of all-cause mortality in men under age 65 years, but in women no evidence is provided to support the notion that risk of overall mortality is related to BMI. Because few participants reported very low BMI levels, we were unable to rule out the possibility that such individuals were at increased risk of death. Despite favorable trends in CHD mortality (5), the disease remains the leading cause of death in the United States (40). Given that approximately one third of American adults are described as being at least 20 percent above desirable body weight and that the trend is worsening (9), these findings have strong public health implications regarding both the prevention and treatment of obesity in men and women.

ACKNOWLEDGMENTS

Supported by the National Heart, Lung, and Blood Institute First Independent Research Support and Transition Award (R29) grant HL5487402.

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