

Original Contribution

Month of Conception and Learning Disabilities: A Record-Linkage Study of 801,592 Children

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Learning disabilities have profound, long-lasting health sequelae. Affected children born over the course of 1 year in the United States of America generated an estimated lifetime cost of \$51.2 billion. Results from some studies have suggested that autistic spectrum disorder may vary by season of birth, but there have been few studies in which investigators examined whether this is also true of other causes of learning disabilities. We undertook Scotland-wide record linkage of education (annual pupil census) and maternity (Scottish Morbidity Record 02) databases for 801,592 singleton children attending Scottish schools in 2006–2011. We modeled monthly rates using principal sine and cosine transformations of the month number and demonstrated cyclicity in the percentage of children with special educational needs. Rates were highest among children conceived in the first quarter of the year (January–March) and lowest among those conceived in the third (July–September) (8.9% vs 7.6%; $P < 0.001$). Seasonal variations were specific to autistic spectrum disorder, intellectual disabilities, and learning difficulties (e.g., dyslexia) and were absent for sensory or motor/physical impairments and mental, physical, or communication problems. Seasonality accounted for 11.4% (95% confidence interval: 9.0, 13.7) of all cases. Some biologically plausible causes of this variation, such as infection and maternal vitamin D levels, are potentially amendable to intervention.

developmental disabilities; educational status; intellectual disabilities; obstetric delivery; seasonal variation

Abbreviations: ASD, autistic spectrum disorder; CI, confidence interval.

Some environmental exposures, such as infection and vitamin D level, follow seasonal patterns. Fetal development represents a unique period of vulnerability to environmental perturbations, and there are multiple pathways via which season of fetal development could plausibly impact long-term outcomes, in particular those associated with abnormal brain development. In several studies, researchers have demonstrated a higher risk of schizophrenia among people born during winter months (1). Studies of neurodevelopmental disorders have been fewer in number, have been largely restricted to autistic spectrum disorder (ASD), and have produced contradictory results. Seasonal patterns for ASD have been demonstrated in some studies (2–9) but not in others (10–13). In the present study, our aim was to determine whether a child's risk of having special

educational needs varies by month of conception and, if so, whether seasonality is restricted to specific causes of special educational needs, such as ASD.

METHODS

Pupil census

Information on special educational needs and their causes was obtained from anonymous, routinely collected educational data. In Scotland, an annual pupil census is conducted among all children who are attending local authority-maintained or grant-aided schools. It covers both primary and secondary schools and includes mainstream schools, special schools, and special classes/units attached

to mainstream schools. Special schools are specifically designed to provide education to children with profound and complex disabilities whose needs cannot be met in mainstream schools. According to data from the 2011 Scottish Census, 99% of children with learning disabilities aged 5–16 years are in some form of education. Children on long-term illness absence are also included in the pupil census.

The information collected includes whether the schoolchild has a record of special educational needs, which is defined as being unable to benefit fully from school education without help beyond that normally given to schoolchildren of the same age. Both schools and local authorities have a statutory duty to identify children with special educational needs, provide support, and review its provision. We included special educational needs attributed to intellectual disabilities, dyslexia, other specific learning difficulties, visual impairment, hearing impairment, deafness and blindness individually combined, physical or motor impairments, language or speech disorder, ASD, and social, emotional, and behavioral difficulties. We excluded children with special educational needs due to bereavement or interrupted learning, as well as more able pupils and young caregivers. Young caregivers are defined as individuals 18 years of age or younger who help to look after a relative who requires support due to disability, illness, mental health problems, or drug or alcohol abuse. Schoolchildren who contributed to more than 1 annual pupil census were classified as having special educational needs if it was recorded in any year.

Maternity database

The Scottish Morbidity Record 02 collects information on all women discharged from Scottish maternity hospitals. Gestational age at delivery, sex, and absolute birthweight were used to derive sex- and gestation-specific birthweight percentiles within the study population. Date of conception was derived from date of delivery minus gestational age at delivery plus 2 weeks. Children's postcodes of residence at the time of delivery were used to determine their level of socioeconomic deprivation using the Scottish Index of Multiple Deprivation (14). It is derived from 38 indicators across 7 domains (income; employment; health; housing; geographic access; crime; and education, skills, and training), using information collected at the level of data zone of residence (median population, 769). The Scottish Index of Multiple Deprivation was then categorized into quintiles for the Scottish population as a whole, from 1 (most deprived) to 5 (least deprived).

Inclusion and exclusion criteria

Record linkage was undertaken using probabilistic matching based on date of birth, sex, and postcode of residence. The linkage methodology has been reported and validated previously and has been shown to be 99% accurate for singleton children (15). Inclusion in the present study was restricted to children who attended school during any of the academic years from 2006/2007 to 2011/2012 inclusive. We excluded individuals who were younger than

4 years of age or older than 19 years of age at the time of the pupil census and individuals for whom maternal age was recorded as younger than 10 years, birth weight was recorded as less than 400 g or greater than 6,500 g, or gestational age at delivery was recorded as less than 24 weeks or greater than 44 weeks. Multiple births were excluded because, in the absence of the children's names, we could not ensure that the pupil census record was linked to the correct child.

Statistical analyses

Since 2006, children with more than 1 type of special educational need have had all types recorded. Therefore, children could contribute to the analyses of more than 1 type of special educational need. Continuous variables were summarized using the median and interquartile range and compared using the Kruskal-Wallis tests. Categorical data were summarized using frequencies and percentages and compared using Pearson χ^2 tests. We modeled the monthly rates using principal sine and cosine transformations of the month number. Statistical significance was assessed using a likelihood ratio test for the sine and cosine terms and, for causes that demonstrated a seasonal pattern, we superimposed the cosinor curve on figures. We calculated the mean monthly incidence over the entire study period and the percentage deviation from the mean for each calendar month. The total seasonal variation was derived by summing the deviation from the mean for the peak and trough months. For further analyses, month of delivery was categorized into quarters, which were selected to reflect the peak and trough months: quarter 1, January–March; quarter 2, April–June; quarter 3, July–September; and quarter 4, October–December.

The characteristics that varied by both calendar year quarter of conception and presence or absence of special educational needs were treated as potential confounders or mediators in the subsequent analyses, and multivariable analysis was performed using binary logistic regression. The *P* values for all hypothesis tests were 2-sided, and actual *P* values are quoted. All analyses were performed using Stata, version 14.1 (StataCorp LP, College Station, Texas). Approval to undertake the study was granted by the Public Benefit and Privacy Panel.

RESULTS

The pupil censuses undertaken between 2006 and 2011 collected data on 1,011,585 children. Of these, 811,860 (80.3%) could be linked to Scottish maternity records. We excluded 10,268 children from the study: 8,585 (83.7%) were not singleton births; 41 (0.4%) had an estimated gestational age at delivery of less than 24 weeks or greater than 44 weeks; 1,096 (10.7%) had missing data on gestational age at delivery; 486 (4.7%) were born at 24–44 weeks' gestation but had a birthweight less than 400 g or greater than 6,500 g; 49 (0.5%) were younger than 4 or older than 19 years of age at the time of the pupil census; and 11 (0.1%) had a maternal age recorded as younger than 10 years. Therefore, the study population comprised

801,592 children. Of these, 66,786 (8.3%) children had at least 1 record of a special educational need: 7,937 (1.0%) had ASD; 17,942 (2.2%) had intellectual disabilities; 37,319 (4.7%) had learning difficulties; 4,360 (0.5%) had sensory impairment; 10,391 (1.3%) had communication problems; 6,401 (0.8%) had physical or motor impairment; 5,814 (0.7%) had physical health problems; and 1,219 (0.2%) had mental health problems. Children with special educational needs differed from those without in relation to many maternal and pregnancy characteristics (Table 1).

The monthly incidence rates of children with special educational needs were plotted by month of conception, and there were clear seasonal patterns for overall special educational needs, ASD, intellectual disabilities, and learning difficulties (Figure 1). There was no clear evidence of a seasonal pattern for physical/motor impairments, physical health, sensory problems, mental health, or communication problems. The likelihood ratio tests of the principal sine and cosine terms in the regression models varied univariately by month of conception for all special educational needs, ASD, intellectual disabilities, and learning difficulties (Table 2). The cosinor models have been superimposed on Figure 1. Overall, special educational needs demonstrated a peak in February and a trough in July/August (Table 2). Therefore, the calendar year was categorized into quarters in subsequent analyses.

The prevalence of special educational needs was highest among children conceived in calendar year quarter 1 and lowest in those conceived in quarter 3 overall (8.9% vs 7.6%; $P < 0.001$) and for ASD (1.0% vs 0.9%; $P = 0.002$), intellectual disabilities (2.4% vs 2.0%; $P < 0.001$), and learning difficulties (5.1% vs 4.1%; $P < 0.001$). There were differences between children with and without special educational needs in terms of maternal age, socioeconomic deprivation quintile, parity, pre-eclampsia, and previous spontaneous abortion and child's gestational age at delivery, sex- and gestation-specific birthweight percentile, and mode of delivery (Table 1). These factors also varied by month of conception. Therefore, these were treated as potential confounders or mediators. Adjusting for these covariates plus year of conception in the multivariable binary logistic models had minimal effect on the associations (Table 3). The population attributable percentages were 11.4% (95% confidence interval (CI): 9.0, 13.7) for any special educational needs; 14.9% (95% CI: 11.8, 18.0) for learning difficulties; 15.1% (95% CI: 10.6, 19.5) for intellectual disabilities; and 11.7% (95% CI: 4.6, 18.3) for ASD.

We re-ran the models including only the 246,594 (30.8%) children who were born at 40 weeks' gestation. The incidence of overall special educational needs displayed a clear seasonal pattern by month of conception ($P < 0.001$), with a peak in February, a trough in August, and a total monthly variation of 2.8%. The percentage of children who developed special educational needs was 8.7% among those conceived in quarter 1 compared with 6.9% among those conceived in quarter 3 ($P < 0.001$). Compared with children conceived in quarter 3, the overall risk of special educational needs was higher among those conceived in quarter 1 (adjusted odd ratio = 1.20, 95%

CI: 1.15, 1.25; $P < 0.001$), quarter 2 (adjusted odds ratio = 1.09, 95% CI: 1.05, 1.14; $P < 0.001$), and quarter 4 (adjusted odds ratio = 1.12, 95% CI: 1.07, 1.17; $P < 0.001$).

DISCUSSION

There was marked variation in the risk of special educational needs in relation to the month of conception. This variation was not dependent on data-driven selection of reference and exposure categories, because the sine and cosine terms of month of conception demonstrated strong associations with the risk of special educational needs. Previous studies have generated inconsistent findings in relation to ASD, but the majority of high-quality studies have shown associations (2–9, 16, 17). Only 11.9% of Scottish schoolchildren with a record of special educational needs had ASD; however, we also found the same pattern of association with learning difficulties and intellectual disabilities. Collectively, the diagnoses that showed seasonal variation accounted for 86.9% of children with special educational needs. Moreover, analysis by attributable fraction indicated that 11.4% of all cases could potentially be prevented if the risk throughout the year was reduced to that observed in quarter 3. In the United States, the lifetime costs associated with children born with intellectual disabilities over the course of 1 year have been estimated to be approximately \$51.2 billion (18). Therefore, preventing 11.4% of cases could save approximately \$5.8 billion in the United States alone. Hence, we showed that seasonal variation in the month of conception is a major and previously unrecognized determinant of a substantial proportion of the economic burden resulting from learning disabilities.

The findings persisted after adjustment for potential confounders, and the lack of a seasonal pattern in sensory, communication, physical, and motor causes of special educational needs demonstrates the specificity of the associations and suggests that they are unlikely to reflect residual confounding. The reported incidence of ASD has increased over time because of increased awareness. However, adjustment for year of conception did not alter the results. Subgroup analysis of children born at 40 weeks' gestation confirmed the same pattern of risk in relation to month of conception. Hence, the patterns observed are suggestive of an environmental exposure that occurs at a critical developmental stage before labor and delivery rather than secondary to seasonal variation in the gestational age at delivery. The nature of the present study does not allow us to determine the mechanism of association. However, 2 plausible exposures that demonstrate seasonal cyclicity have been previously implicated in the etiology of ASD, namely maternal infection and maternal vitamin D levels.

Results from animal models support an effect of maternal infection on the neurodevelopment of the offspring. Exposure of pregnant mice to influenza virus has both short-term and long-lasting deleterious effects on the developing brain structure in the progeny (19). The resultant changes include abnormal corticogenesis, which is associated with the development of abnormal behavior in mice

Table 1. Characteristics of Study Participants by Presence or Absence of Special Educational Needs, Scotland, United Kingdom, 2006–2011

Characteristic	No Special Educational Needs (<i>n</i> = 734,806)		Special Educational Needs (<i>n</i> = 66,786)		<i>P</i> Value
	No.	% ^a	No.	% ^a	
Sex					<0.001
Female	368,620	50.2	22,463	33.6	
Male	366,162	49.8	44,316	66.4	
Missing	24		7		
Deprivation quintile					<0.001
1 (most deprived)	193,257	26.4	20,957	31.5	
2	151,592	20.7	14,706	22.1	
3	135,066	18.4	12,242	18.4	
4	128,668	17.6	10,384	15.6	
5 (least deprived)	123,727	16.9	8,324	12.5	
Missing	2,496		173		
Parity					<0.001
Nulliparous	333,337	45.6	26,769	40.3	
Multiparous	398,321	54.4	39,676	59.7	
Missing	3,148		341		
Pre-eclampsia					<0.001
No	713,668	97.1	64,633	96.8	
Yes	21,138	2.9	2,153	3.2	
Missing	0		0		
Previous therapeutic abortion					<0.001
0	656,604	89.4	58,702	87.9	
1	66,624	9.1	6,666	10.0	
≥2	11,484	1.6	1,404	2.1	
Missing	94		14		
No. of previous spontaneous abortions					<0.001
0	592,357	80.6	52,303	78.3	
1	110,377	15.0	10,869	16.3	
≥2	31,971	4.4	3,599	5.4	
Missing	101		15		
Gestational age at delivery, weeks					<0.001
24–36	38,816	5.3	5,820	8.7	
37	34,745	4.7	3,881	5.8	
38	91,040	12.4	9,040	13.5	
39	149,272	20.3	13,400	20.1	
40	227,798	31.0	18,796	28.1	
41	162,713	22.1	13,372	20.0	
42	29,433	4.0	2,419	3.6	
43	833	0.1	48	0.1	
44	156	0.0	10	0.0	
Missing	0		0		
Sex- and gestation-specific birthweight percentile					<0.001
1–3	21,639	2.9	3,178	4.8	
4–10	51,110	7.0	5,789	8.7	
11–20	73,487	10.0	7,597	11.4	
21–80	443,545	60.4	38,336	57.4	

Table continues

Table 1. Continued

Characteristic	No Special Educational Needs (n = 734,806)		Special Educational Needs (n = 66,786)		P Value
	No.	% ^a	No.	% ^a	
81–90	71,840	9.8	5,698	8.5	
91–97	51,438	7.0	4,324	6.5	
98–100	21,723	3.0	1,857	2.8	
Missing	24		7		
Mode of delivery					<0.001
Cephalic vaginal	506,585	68.9	45,870	68.7	
Assisted vaginal	88,413	12.0	6,920	10.4	
Breech vaginal	2,442	0.3	311	0.5	
Elective caesarean	51,016	6.9	4,822	7.2	
Emergency caesarean	86,182	11.7	8,851	13.3	
Other	167	0.0	12	0.0	
Missing	1		0		
Maternal age, years ^b	28 (24–32)		28 (23–32)		<0.001

^a Persons with missing data were excluded from the percentage calculations.

^b Values are expressed as median (interquartile range).

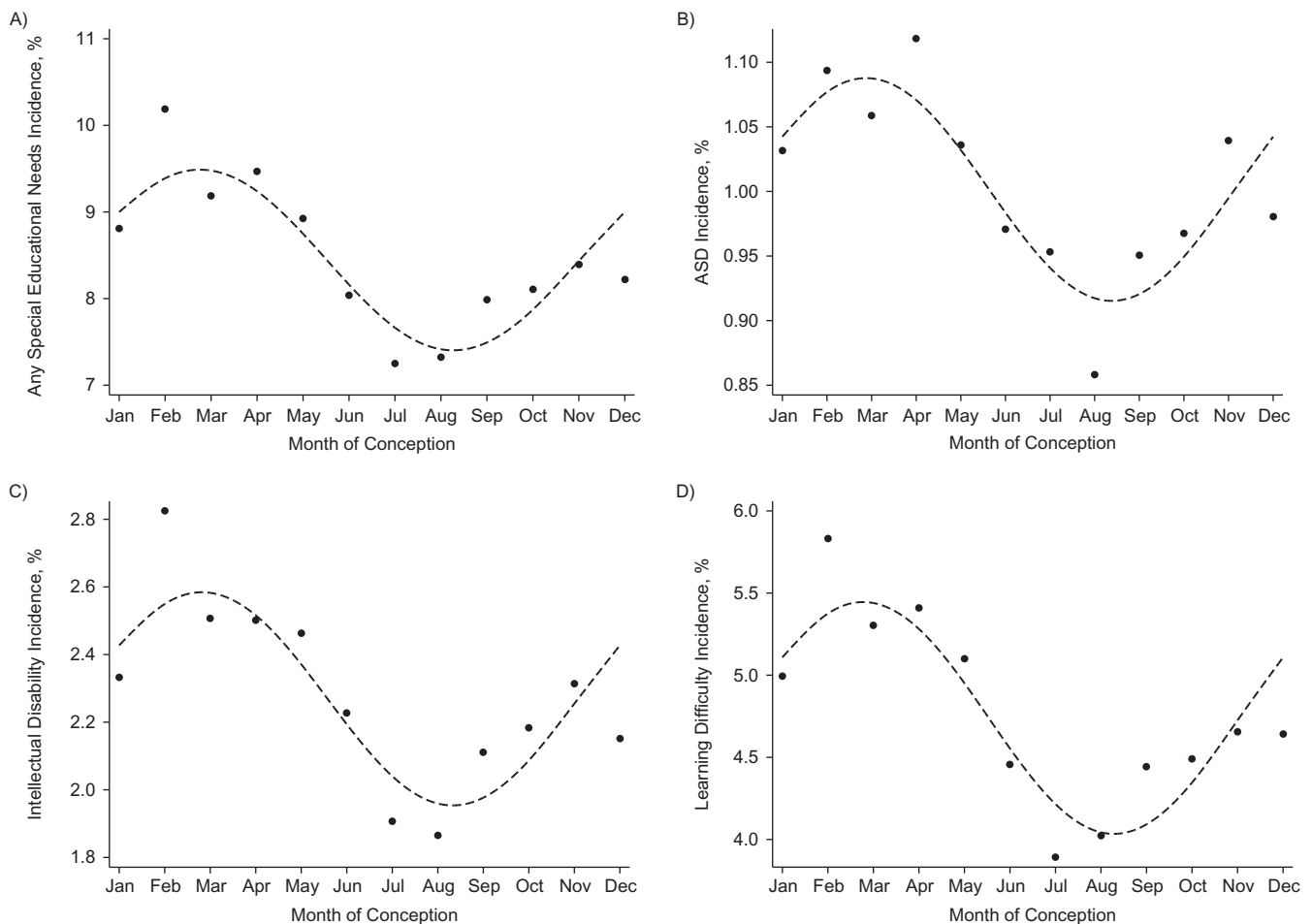


Figure 1. Crude monthly incidence (dots) and pure cosinor models (dashed lines) of additional educational support needs, Scotland, United Kingdom, 2006–2011.

Table 2. Percentage by Which Monthly Incidence of Special Educational Needs, Overall and by Cause, Deviated From Overall Incidence, Scotland, United Kingdom, 2006–2011

Special Educational Need	January	February	March	April	May	June	July	August	September	October	November	December	Total Variation ^a	P Value ^b
All	0.32	1.70	0.70	0.98	0.44	-0.45	-1.24	-1.17	-0.51	-0.39	-0.10	-0.27	2.94	<0.001
ASD	0.03	0.09	0.05	0.11	0.03	-0.03	-0.05	-0.15	-0.05	-0.04	0.03	-0.02	0.24	<0.001
Intellectual disabilities	0.05	0.54	0.22	0.22	0.18	-0.06	-0.38	-0.42	-0.17	-0.10	0.03	-0.13	0.96	<0.001
Learning difficulties	0.22	1.06	0.53	0.64	0.33	-0.31	-0.88	-0.75	-0.33	-0.28	-0.12	-0.13	1.94	<0.001
Sensory impairment	0.01	0.08	-0.01	0.06	0.02	-0.05	-0.02	0.00	0.01	0.00	-0.04	-0.06	0.14	0.419
Communication problems	0.00	0.13	0.01	0.04	0.06	-0.09	-0.03	-0.12	0.01	-0.04	0.07	-0.02	0.25	0.042
Physical/motor impairment	0.01	0.13	0.04	0.02	-0.02	-0.02	-0.10	-0.04	-0.02	0.06	-0.01	-0.06	0.23	0.077
Physical health problems	0.01	0.03	0.01	0.04	0.01	0.00	-0.04	0.02	-0.04	0.00	-0.03	0.00	0.08	0.046
Mental health problems	0.01	-0.01	0.02	0.01	0.01	0.00	0.00	-0.04	-0.02	0.03	-0.01	0.00	0.07	0.133

Abbreviation: ASD, autistic spectrum disorder.

^a Sum of highest and lowest deviations.^b Derived from likelihood ratio test of principal sine and cosine terms in regression models for each outcome.

(20). In wild-type mice, maternal immune activation of pregnant rodents produces offspring with abnormalities in behavior, histology, and gene expression that are similar to schizophrenia and ASD. However, this does not occur in the interleukin 6–null mutant animals, suggesting that interleukin 6 may lie on the causal pathway. The results from human studies have been inconsistent. Atladóttir et al. (21) studied all children born in Denmark between 1980 and 2005. They found no overall association between maternal infection during pregnancy and ASD but observed a higher risk of ASD associated with maternal viral infection during the first trimester and bacterial infection during the second trimester. In a case-control study that included 538 children with ASD and 163 with developmental delays, Zerbo et al. (22) demonstrated associations of both conditions with fever during pregnancy. In a further case-control study, investigators found that both ASD and developmental delay were associated with elevated second trimester levels of a number of cytokines in the mother's blood (23). In a study of 689,196 births in Denmark, there was a higher risk of ASD among children whose mothers suffered from autoimmune diseases, such as rheumatoid arthritis and celiac disease (24). Not all studies have shown positive associations, and an analysis of the English autism register relating to births between 1953 and 1988 demonstrated no increases in autism cases coinciding with influenza epidemics (25).

Maternal serum levels of vitamin D are important for normal brain development and demonstrate marked seasonal changes because the majority of vitamin D is derived from exposure to sunlight (26). Low concentrations have been associated with changes in brain size and morphology (27, 28). Animal models have demonstrated that offspring deficient in vitamin D late in pregnancy or across the whole of pregnancy displayed adult brain dysfunction and hyperlocomotion. Low exposure to ultraviolet radiation has been put forth as a possible explanation for the higher incidence of ASD in countries at high latitudes, urban areas, and dark-skinned people (26). Whitehouse et al. (29) measured 25-dihydroxyvitamin D concentrations in 743 white mothers at 18 weeks' gestation. They found an association with language impairment in offspring at 5 and 10 years of age. Swedish investigators measured 25-hydroxyvitamin D in the dried blood spots obtained from children shortly after birth (30). They found lower levels in 58 children with ASD than in their siblings. Intervention studies conducted in early childhood have shown that administration of multivitamins containing vitamin D can reduce symptoms in children with ASD (31) and improve normal childhood cognition (32).

There is a well-established link between vitamin D and autoimmunity. In a systematic review, Yang et al. (33) demonstrated that the vitamin D receptor is located on many immune cell lines, enabling vitamin D to moderate the relationship between normal immunological function and development of autoimmune disease. Dopico et al. (34) recently demonstrated seasonal variations in more than 4,000 protein-coding messenger RNAs in white blood cells and adipose tissues that resulted in seasonal variations in immunological markers such as interleukin 6 and C-reactive protein.

In most previous studies, investigators have examined month of delivery rather than month of conception. However,

Table 3. Univariable and Multivariable Binary Logistic Regression Models of the Association Between Calendar Year Quarter of Conception and Special Educational Needs, Overall and by Cause, Additionally Adjusted for Calendar Year of Conception, Scotland, United Kingdom, 2006–2011

Special Educational Need	Univariate Model									Multivariable ^a Model								
	Quarter 1			Quarter 2			Quarter 4			Quarter 1			Quarter 2			Quarter 4		
	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value
All	1.20	1.17, 1.22	<0.001	1.14	1.11, 1.16	<0.001	1.11	1.08, 1.13	<0.001	1.19	1.16, 1.22	<0.001	1.12	1.10, 1.15	<0.001	1.11	1.08, 1.14	<0.001
ASD	1.10	1.04, 1.18	0.002	1.09	1.02, 1.16	0.008	1.08	1.02, 1.15	0.013	1.10	1.03, 1.17	0.003	1.08	1.02, 1.15	0.015	1.11	1.02, 1.16	0.012
Intellectual disabilities	1.23	1.18, 1.29	<0.001	1.18	1.13, 1.23	<0.001	1.13	1.09, 1.18	<0.001	1.23	1.18, 1.29	<0.001	1.17	1.12, 1.22	<0.001	1.13	1.09, 1.18	<0.001
Learning difficulties	1.23	1.19, 1.27	<0.001	1.16	1.13, 1.20	<0.001	1.12	1.09, 1.16	<0.001	1.23	1.20, 1.27	<0.001	1.15	1.12, 1.19	<0.001	1.13	1.09, 1.16	<0.001
Sensory impairment	1.01	0.93, 1.10	0.858	0.99	0.91, 1.08	0.879	0.95	0.88, 1.04	0.283	1.00	0.92, 1.09	0.987	0.98	0.90, 1.06	0.568	0.96	0.88, 1.04	0.314
Physical/motor impairment	1.09	1.02, 1.17	0.013	1.04	0.97, 1.11	0.314	1.07	1.00, 1.14	0.067	1.08	1.01, 1.16	0.026	1.01	0.94, 1.09	0.689	1.07	1.00, 1.15	0.065
Communication problems	1.06	0.99, 1.11	0.056	1.02	0.96, 1.07	0.594	1.04	0.99, 1.10	0.127	1.02	0.96, 1.07	0.597	0.98	0.93, 1.04	0.551	1.05	0.99, 1.11	0.102
Physical health problems	1.07	0.99, 1.15	0.071	1.04	0.97, 1.12	0.295	1.01	0.94, 1.09	0.750	1.06	0.98, 1.14	0.142	1.03	0.95, 1.11	0.489	1.01	0.94, 1.09	0.779
Mental health problems	1.17	0.99, 1.38	0.059	1.18	1.00, 1.38	0.051	1.21	1.03, 1.42	0.020	1.16	0.98, 1.37	0.077	1.15	0.98, 1.36	0.087	1.21	1.03, 1.42	0.021

Abbreviations: ASD, autistic spectrum disorder; CI, confidence interval; OR, odds ratio.

^a Adjusted for sex, maternal age, socioeconomic deprivation quintile, parity, pre-eclampsia, previous spontaneous and therapeutic abortion, gestational age at delivery, and sex- and gestation-specific birthweight percentile and year of conception.

variations in gestational age at delivery make it difficult to draw conclusions about which trimester may be most critical in terms of seasonally patterned exposures. By studying month of conception, we could be certain of the calendar months covered by the first and second trimesters in the whole study population, and in the subgroup analysis of children born at 40 weeks' gestation, we could be certain of the months covered by the third trimester as well as, obviating any bias due to known seasonal variations in the risk of pre-term delivery.

Our study was large and nonselective, including children in public schools across the whole of Scotland. The pupil census does not include private schools but, in Scotland, fewer than 5% of children attend private schools. We were able to examine a range of causes of special educational needs and therefore to explore whether seasonal patterning was specific to 1 or more causes. We used existing databases, but these are subjected to regular quality-assurance checks. The proportion of children recorded as having ASD in the pupil census has progressively risen year to year over the past decade because of improved awareness and better diagnostic services, and it reached 1.7% in the most recent (2015) pupil census. Consequently, for the period of our study, 2006–2011, the children recorded as having ASD are likely to be those at the more severe end of the spectrum. For other types of special educational needs, the prevalence derived from the pupil census was very similar to that reported in the 2011 Scottish Census.

Twenty percent of children could not be linked to a maternity record. According to the 2011 Scottish Census, 11% of Scottish residents aged 5–19 years were born outside of Scotland and thus should not be linkable to Scottish maternity records. Therefore, 9% of Scottish schoolchildren were born in Scotland but could not be linked to their maternity record. We previously undertook a validation study of the pupil census–Scottish Morbidity Record 02 linkage process and demonstrated that more than 99% of the linkages that were made attached the child to the correct maternity record (14). We compared the pupil census data for linked and unlinked children and found very similar prevalence of any special educational needs (8% vs. 7%), ASD (both 1%), intellectual disabilities (both 2%), and learning difficulties (4% vs. 5%). Adjustment for birth weight and gestational age at delivery made little difference to the results, which suggests that very little, if any, of the association between month of conception and learning difficulties is mediated via these factors.

A relative weakness of the present study is that we lacked biological samples to test potential etiological hypotheses directly. We were unable to relate the risk of special educational needs to serologically proven viral infections or maternal values of vitamin D. Further studies will be required to address this issue. The timing of the peaks and troughs were, however, consistent with an infectious link. The study by Atladóttir et al. suggested that the first trimester may be a critical period for exposure to viral infection (21). In the United Kingdom, the incidence of influenza is highest between January and March (35), which was the timing of conception associated with the highest risk of special educational needs. The patterns observed were also consistent with ultraviolet

exposure-dependent changes in maternal vitamin D levels playing a role. Results from a mouse model suggested that late gestation may be a critical period for vitamin D (36). In contrast, our study suggests that if ultraviolet radiation does play a role in humans, the first trimester may be the critical period. In the United Kingdom, there is insufficient ultraviolet B radiation in sunlight between November and March to produce vitamin D (26). In our study, the incidence of special educational needs peaked among children conceived in February whose mothers would have experienced low levels of ultraviolet B radiation and therefore produced low levels of vitamin D in early pregnancy and experienced higher levels in late pregnancy. Conversely, the incidence of special education needs was lowest among children conceived in July and August who would have experienced high levels of vitamin D in their first trimester and low levels in their third trimester.

In conclusion, we demonstrated that season of conception is strikingly associated with the subsequent risk of special educational needs in the offspring. The patterns observed were consistent with putative biological explanations of seasonal variation, namely infection exposure during the first trimester and reduced ultraviolet exposure in the first trimester. Because seasonal variability accounts for a substantial health economic burden of disease and biologically plausible causes of this variation are potentially amenable to intervention, these observations are potentially highly relevant for public health.

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