Month of conception and learning disabilities: A record-linkage study of 801,592 children.

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Running title: Month of conception and learning disabilities

Abbreviations: ASD, autistic spectrum disorder; CI, confidence interval; Q, quarter; UV, ultra-violet

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Abstract

Learning disabilities have profound, long-lasting health sequelae. Affected children born over one year in the United States of America generated an estimated lifetime cost of $51.2 billion. Studies suggest autistic spectrum disorder may vary by season of birth, but few studies have 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 2006-2011. We modelled monthly rates using principal sine and cosine transformations of the month number, and demonstrated cyclicity in the percentage of children with special educational needs; highest among children conceived in the first quarter (January-March) and lowest 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 (eg dyslexia), and were absent for sensory or motor/physical impairments, and mental, physical or communication problems. Seasonality accounted for 11.4% (95% confidence interval (CI) 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.

Key terms

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

Introduction

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

Ascertainment of special educational needs and its cause was obtained from anonymous, routinely collected educational data. In Scotland, an annual pupil census is conducted of 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; 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, deaf-blind, physical or motor impairments, language or speech disorder, ASD, and social, emotional and behavioural difficulties. We excluded special educational needs due to bereavement or interrupted learning as well as more able pupils and young carers. Young carers are defined as individuals aged 18 years or under 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 one 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. Gestation at delivery, sex and absolute birthweight were used to derive sex-, gestation-specific birthweight centiles within the study population. Date of conception was derived from date of delivery minus gestational age at delivery plus two 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 datazone of residence (median population 769). The Scottish Index of Multiple Deprivation is then categorised 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 shown to be 99% accurate for singleton children (15). Inclusion in this study was restricted to children who attended school during any of the academic years 2006/2007 to 2011/2012 inclusive. We excluded individuals who were aged <4 years or >19 years at the time of the pupil census and individuals for whom maternal age was recorded as less than 10

years, birth weight was recorded as less than 400g or greater than 6,500g, or gestation 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 one type of special educational needs have had all types recorded. Therefore, children could contribute to the analyses of more than one type of special educational needs. Continuous variables were summarised using the median and inter-quartile range and compared using Kruskal-Wallis tests. Categorical data were summarized using frequencies and percentages and compared using Pearson chi-square tests. We modelled 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 which 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 summating the deviation from the mean for the peak and trough months. For further analyses, month of delivery was categorised into quarters selected to reflect the peak and trough months: Quarter (Q) 1 (January-March); Q2 (April-June); Q3 (July-September); and Q4 (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 two-sided and actual p values are

quoted. All analyses were performed using Stata 14.1 (StataCorp LP, Austin, 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 gestation at delivery of <24 weeks or >44 weeks; 1,096 (10.7%) had missing data on gestation at delivery; 486 (4.7%) were born at 24-44 weeks gestation but had a birthweight <400 or >6,500 grams; 49 (0.5%) were aged <4 or >19 years at the time of the pupil census; and 11 (0.1%) had maternal age recorded as <10 years. Therefore, the study population comprised 801,592 children. Of these, 66,786 (8.3%) children had at least one record of special educational need: 7,937 (1.0%) ASD; 17,942 (2.2%) intellectual disabilities; 37,319 (4.7%) learning difficulties; 4,360 (0.5%) sensory impairment; 10,391 (1.3%) communication problems; 6,401 (0.8%) physical/motor impairment; 5,814 (0.7%) physical health problems; and 1,219 (0.2%) 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 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) and 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 categorised into quarters in subsequent analyses: Q1 (January-March); Q2 (April-June); Q3 (July-September) and Q4 (October-December).

The prevalence of special educational needs was highest among children conceived in calendar year Q1 and lowest in Q3: overall (8.9% vs 7.6%, p<0.001), 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, previous spontaneous abortion, gestational age at delivery, sex- gestation-specific birthweight centile 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 the peak in February and trough in August and a total monthly variation of 2.8%. The percentage of children who developed special educational needs was 8.7% for those conceived in Q1 compared to 6.9% for those conceived in Q3 (p<0.001). Compared to children conceived in Q3, the overall risk of special educational needs was higher among those conceived in Q1 (adjusted OR 1.20, 95% CI 1.15,

1.25, p<0.001), Q2 (adjusted OR 1.09, 95% CI 1.05, 1.14, p<0.001) and Q4 (adjusted OR 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, as 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 which 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 Q3. In the USA, the lifetime costs associated with children born over one year with intellectual disabilities have been estimated to be around $51.2 billion (18). Therefore, preventing 11.4% of cases could save around $5.8 billion in the USA alone. Hence, we showed that seasonal variation in the month of conception is a major and previously unrecognised determinant of a substantial proportion of the economic burden resulting from learning disability.

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 demonstrate the specificity of the associations and suggests that they are unlikely to reflect residual confounding. The reported incidence of ASD has increased over time, due to increased awareness. However, adjustment for year of conception did not alter the results. Sub-group analysis of children born at 40 weeks 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 prior to labour 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, two plausible exposures which demonstrate seasonal cyclicity have been previously implicated in the aetiology of ASD, namely maternal infection and maternal vitamin D levels.

Animal models support an effect of maternal infection on the neurodevelopment of the offspring. Exposure of pregnant mice to influenza virus has both short and long lasting deleterious effects on the developing brain structure in the progeny (19). The resultant changes include abnormal corticogenesis which is associated with development of abnormal behaviour in mice (20). In wild-type mice, maternal immune activation of pregnant rodents produces offspring with abnormalities in behaviour, histology, and gene expression which 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 of human studies are inconsistent. Atladottir et al. studied all children born in Denmark between 1980 and 2005 (21). They found no overall association between maternal infection during pregnancy and ASD but observed an increased risk of ASD associated with maternal viral infection during the first trimester and bacterial infection during the second trimester. A case control study including 538 children with ASD and 163 with developmental delays demonstrated associations between both conditions and fever during pregnancy (22). A further case control study 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 an increased risk of ASD among children

whose mothers suffered from autoimmune diseases such as rheumatoid arthritis and coeliac 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, as 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 mooted as a possible explanation for the higher incidence of ASD in high latitude countries, urban areas and dark-skinned people (26). Whitehouse et al. measured 25-dihydroxyvitamin D concentrations in 743 Caucasian mothers at 18 weeks gestation. They found an association with language impairment at 5 and 10 years of age (29). 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 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. A systematic review by Yang et al. 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 (33). Copico et al. recently demonstrated seasonal variations in more than 4,000 protein-coding mRNAs in white blood cells and adipose tissues

resulting in seasonal variations in immunological markers such as interleukin 6 and C reactive protein (34).

Most previous studies have examined month of delivery, rather than month of conception. However, variations in gestation 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 sub-group analysis of children born at 40 weeks gestation, we could also 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 preterm delivery.

Our study was large and non-selective, 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 one 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 on year over the last decade, due to improved awareness and better diagnostic services, and 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, therefore, 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 gestation of delivery made little difference to the results suggesting 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 aetiological 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 Atladottir 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 (UV) exposure dependent changes in maternal vitamin D levels playing a role. A mouse model suggested that late gestation may be a critical period for vitamin D (36). In contrast, our study suggests that, if UV radiation does play a role in humans, the first trimester may be the critical period. In the United Kingdom, there is

insufficient UVB 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 UVB 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 UV exposure in the third trimester. As seasonal variability accounts for a substantial health economic burden of disease and biologically plausible causes of this variation are potentially amendable to intervention, these observations are potentially highly relevant for public health.

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Table 1. Characteristics of study participants by presence or absence of special educational needs

	No special educational needs N=734,806		Special educational needs N=66,786		P value
	No.	**%**	**No.**	**%**	
Sex					
female	368,620	50.2	22,463	33.6	<0.001
male	366,162	49.7	44,316	66.4	
missing	24		7		
Deprivation quintile					
1 (most deprived)	193,257	26.4	20,957	31.5	<0.001
2	151,592	20.7	14,706	22.1	
3	135,066	18.4	12,242	18.4	
4	128,668	17.6	10,834	15.6	
5 (least deprived)	123,727	16.9	8,324	12.5	
missing	2,499		173		
Parity					
nulliparious	333,337	45.6	26,769	40.3	<0.001
multiparous	398,321	54.4	39,676	59.7	
missing	3,148		341		
Pre-eclampsia					
no	713,668	97.1	64,633	96.8	<0.001
Yes	21,138	2.9	2,153	3.2	
missing	0		0		
Previous therapeutic abortion					
0	656,604	89.4	58,702	87.9	<0.001
1	66,624	9.1	6,666	10.0	
≥2	11,484	1.6	1,404	2.1	
missing	94		14		
Previous spontaneous abortion					
0	592,357	80.6	52,303	78.3	<0.001
1	110,377	15.0	10,869	16.3	
≥2	31,971	4.4	3,599	5.4	
missing	101		15		
Gestational age (weeks)					
24-36	38,816	5.3	5,820	8.7	<0.001
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-, gestation-specific birthweight centile					
1-3	21,639	2.9	3,178	4.8	<0.001
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	
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					
cephalic vaginal	506,585	68.9	45,870	65.9	<0.001
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)[a]	28	24-32	28	23-32	<0.001

[a]maternal age expressed as median (inter quartile range)

Table 2. Percentage by which monthly incidence of special educational needs, overall and by cause, deviated from overall incidence.

	January	February	March	April	May	June	July	August	September	October	November	December	Total variation[a]	P value[b]
Special educational needs	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

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

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.

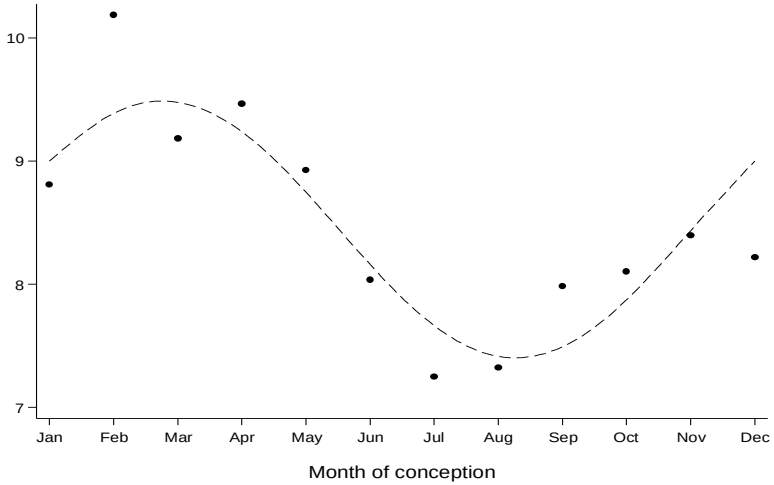
	Univariate						Multivariable[a]					
	Q1		Q2		Q4		Q1		Q2		Q4	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Special educational needs	1.20 (1.17, 1.22)	<0.001	1.14 (1.11, 1.16)	<0.001	1.11 (1.08,1.13)	<0.001	1.19 (1.16, 1.22)	<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

Q quarter; OR odds ratio; CI confidence interval; SEN special educational needs; ASD autistic spectrum disorder

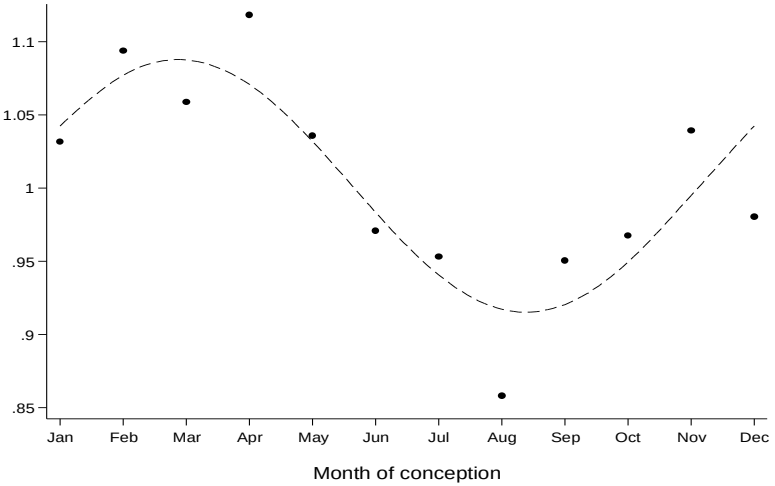
[a]adjusted for sex, maternal age, socioeconomic deprivation quintile, parity, pre-eclampsia, previous spontaneous and therapeutic abortion, gestational age at delivery and sex-, gestation-specific birthweight centile and year of conception

Figure 1. Crude monthly incidence (%) and pure cosinor models of additional educational support needs

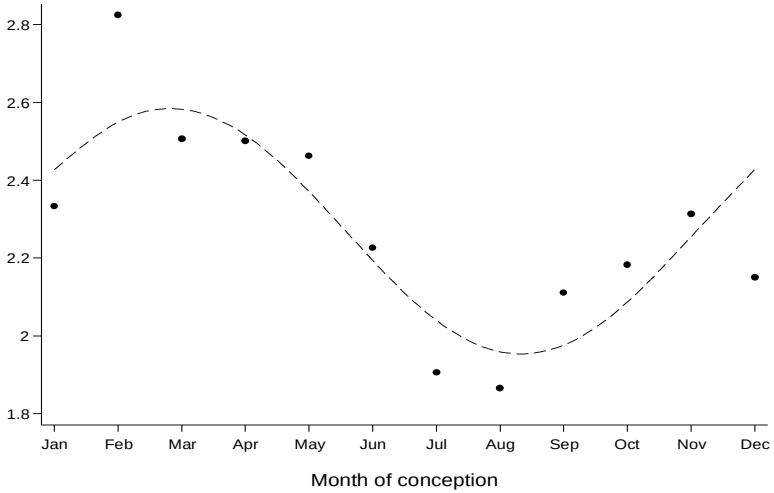
1. Any ASN



2. ASD



3. Intellectual disability



4. Learning difficulty