



Abel, K., Heuvelman, H., Wicks, S., Rai, D., Emsley, R., Gardner, R., & Dalman, C. (2017). Gestational age at birth and academic performance: population-based cohort study. *International Journal of Epidemiology*, 46(1), 324-335. <https://doi.org/10.1093/ije/dyw284>

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Gestational age at birth and academic performance: a population-based cohort study

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Source of support: This work was supported by the Baily Thomas Charitable Fund [TRUST/RNA/AC/KW/3115/5780].

Word count: 3112 words, 5 figures, 1 table, 6 supplements

Ethical approval: Ethical approval for this study was granted by the research ethics committee at Karolinska Institute [2010/1185-31/5 and 2013/1118-32], allowing record linkage without personal consent when the confidentiality of the individuals is maintained. The personal identity of participants was replaced with a serial number before the research group were given access to these data. It is of paramount importance to ensure the protection of the personal integrity against any violations, and legislation regulating the handling of information that is directly or indirectly linked to a person is in place (the Personal Data Act).

Summary

Background: Numerous studies suggest preterm birth is associated with cognitive deficit. However, less is known about cognitive outcomes following post-term birth, or the influence of weight variations within term or post-term populations. We examined associations between gestational age (GA) and school performance, by weight-for-GA, focusing on extremely pre- and post-term births.

Method: Record linkage study of Swedish children born 1973-1994 (n=2 008 102) with a nested sibling comparison (n=439 629). We used restricted cubic regression splines to examine associations between GA and the grade achieved on leaving secondary education, comparing siblings to allow stronger causal inference with regard to associations between GA and school performance.

Results: Grade averages of both pre- and post-term children were below those of full-term counterparts and lower for those born small-for-GA. The adjusted grades of extremely preterm children (at 24 completed weeks), while improving in later study periods, were lower by 0.43 standard deviations (95% confidence interval 0.38 to 0.49), corresponding with a 21 point reduction (19 to 24) on a 240-point scale. Reductions for extremely post-term children (at 45 completed weeks) were lesser (-0.15 SD (-0.17 to -0.13) or -8 points (-9 to -7)). Among matched siblings, we observed weaker residual effects of preterm and post-term GA on school performance.

Conclusions: There may be independent effects of fetal maturation and fetal growth on school performance. Associations among matched siblings, although attenuated, remained consistent with causal effects of pre- and post-term birth on school performance.

Key words: gestational age, academic performance, Sweden, whole-population cohort, siblings, post-term.

Key messages:

- On leaving compulsory secondary education, both pre- and post-term children had lower grades than term counterparts.
- The grades of small-for-gestational age children were lowest irrespective of GA at birth.
- Despite potential familial confounding, there may be residual causal effects of pre- and post-term GA on school-leaving age academic performance.

Introduction

In developed countries, 5% to 7% of births occur preterm (≤ 36 weeks) comprising a major determinant of infant mortality and health [1]. Rates of post-term birth (≥ 42 weeks) vary considerably (0.5% to 8% in Europe and the US), possibly reflecting differences in local obstetric practice [2, 3]. In recent years, change in obstetric practice has resulted in greater numbers of induced deliveries [4], influencing rates of post-term birth over time [5]. Although it is often assumed that term and post-term births are homogeneous with respect to health outcomes, post-term delivery has been associated with infant mortality [6, 7] and longer-term health problems [8–10]. However, while risk of neurodevelopmental problems in preterm infants is well-established [11–21], little is known about risk post-term [11, 18, 22]. Evidence suggests cognitive abilities improve with gestational age (GA) toward term, reaching a peak at 40 weeks before decreasing towards late term [22, 23]. However, most studies remain underpowered to assess whether ability continues to decline with GA post-term [11, 18], or examine the influence of variations in birth weight in post-term populations [11–14, 17, 18, 21, 24–28]. Moreover, it is possible that genetic or shared environmental factors contribute to a non-optimal GA and also influence later cognitive abilities [12]. Such confounding has not yet been examined in post-term children. We used a Swedish whole-population cohort to detail the relationship between GA and school grades across the full range of gestation (22–45 weeks).

Our aims were to: 1) estimate school-leaving grade averages for children born at varying GA, taking account of weight-for-GA; 2) examine associations between GA and school grades, focusing specifically on extremely pre- or post-term children; and 3) explore confounding by unmeasured familial factors among matched siblings.

Method

Study cohort

In the Swedish Medical Birth Register (MBR), we identified live births between 1973 and 1994 (n=2 277 940) and linked these, via the registration number, with the National School Register and other registers from Statistics Sweden and the National Board of Health and Welfare (NBHW). Individuals were linked with parents, who in turn were linked with demographic, socioeconomic and psychiatric data. We excluded (Figure 1) multiple births, children with missing GA or birth weight, implausible combinations of GA and birth weight (Supplement 3), who died or emigrated before 16, had no final grade record, resided abroad within 2 years of attaining their grade, or who could not be linked with parents, leaving 2 008 102 individuals for population-level analyses. To analyse matched siblings, we excluded adoptees, children without full siblings in the cohort, and sex-discordant siblings (excluding the least common sex, or retaining females where numbers equaled), leaving 302 718 same-sex siblings born preterm to term and 136 911 born term to post-term.

(Figure 1 here)

Exposure

A categorical measure of GA distinguished between extremely preterm (22-27 weeks), very preterm (28-31), preterm (32-33), late preterm (34-36), early term (37-39) or full-term (40-41) and those born in any of the post-term weeks (42, 43, 44, 45). We defined GA in days for use in statistical analyses. For the sibling comparison, sibling-averaged GA captured between-family variation in gestational duration ^[29].

Outcome

Academic performance was measured by the final grade achieved on completing secondary education at 16. For those completing before 1998, this was the average across completed subjects (ranging from 1 to 5), while for those completing from 1998 onwards we used the summary score for completed subjects (80 to 320). As this study covers both grading systems, we calculated year- and sex-standardised z-scores based on the original grades to ensure comparability between grading systems (Supplement 1).

Covariates

Data on sex, birth weight (grams), parity (first-born), parental age, birth condition (APGAR ≤ 6), birth complications (Caesarean section, assisted delivery), medical risk factors (gestational diabetes or hypertension, preeclampsia), congenital malformation, and labour induction (for 1990-1994) were extracted from the MBR. Standardising birth weight distributions to sex and number of completed weeks' gestation, we constructed a continuous measure of weight-for-GA, with children in the lower and upper deciles considered small- and large-for-gestational age (SGA/LGA). Parental psychiatric history and diagnoses of intellectual disability were obtained from the National Patient Register, and parental country of birth (Sweden/other) from the Register of the Total Population. We obtained family income around birth from the Income and Taxation Register and the Longitudinal Integration Database for Health Insurance and Labour Market Studies, adjusting for family size, and coding income quintiles as described previously ^[30]. Parental educational achievement (pre-upper-secondary/upper-secondary/post-upper-secondary) and receipt of welfare benefits were obtained for 1990-1994.

Statistical analysis

Analyses were performed in Stata/SE version 12.1. We assessed prevalence of pre- and post-term birth between 1973-1994; calculated grade averages for children born at varying GA and weight-for-GA; compared characteristics by GA ; and examined associations between GA and school performance

in three adjacent study periods (1973-1979, 1980-1986, 1987-1994) to allow change in association over time. We used restricted cubic regression splines to model non-linear associations between GA and school performance. Using *mkspline* ^[31], we calculated seven knots at the 2.5th, 17.5th, 33.3rd, 50th, 66.6th, 82.5th and 97.5th percentiles of the GA distribution (the maximum when knot locations are not specified) delineating the range of GA values included in each spline. We analysed the data using mixed models, specifying a random effect with *xtreg* to take account of within-family correlation in school performance. Covariates (missing for 1%) included weight-for-GA including a quadratic term, birth year, parity, parental age, maternal medical risk, parental psychiatric history, parental country of birth and family income. We calculated effects on school performance (expressed as the expected standard deviation change in school grade) across the full range of GA using *xbrcspline* post-estimation with those born at 40 weeks and 4 days as the referent. We then replaced the continuous weight-for-GA variables with indicators for SGA and LGA birth to assess effects of fetal growth restriction and macrosomia on school performance irrespective of GA, and assessed the size of these effects specifically in those born post-term. We did not control for Apgar, congenital malformation, induced or complicated births as these are potential causal pathway characteristics.

To explore familial confounding, we examined associations after adjustment for sibling-averaged GA. These effects are interpreted as associations between GA and school grades, holding constant the tendency of families to delivery offspring early or late. Sibling-averaged GA therefore acts as a proxy for unmeasured familial traits which may result in non-optimal GA and poorer school performance, providing an estimate of the within-family effect of variation in GA ^[29]. In the absence of, or on adjustment for, sibling non-shared confounders, residual within-family association is consistent with a causal effect of GA on school performance ^[32].

To avoid comparison of preterm siblings (for whom advancing GA is supposedly beneficial) with post-term counterparts (for whom this may be detrimental) we examined two cohorts: one in which all were born preterm to term; the other with term to post-term individuals. Replicating our population-level model, we specified the same knot locations; estimated associations with mixed models; and

calculated effects on school performance across the full range of GA. The influence of sibling non-shared confounders was assessed by including covariates for first-birth, parental age, maternal medical risk factors and family income.

Sensitivity analyses

We assessed whether associations varied by gender, children born with or without congenital abnormalities, or characteristics potentially on the causal pathway (Supplement 3). Individuals with complete socioeconomic data (1989-1994) were examined to assess residual socioeconomic confounding (Supplement 4).

Results

Prevalence of pre- and post-term birth

Preterm delivery (≤ 36 weeks) was stable between 4% and 5% (Figure 2), while post-term delivery (≥ 42 weeks) decreased from 14% to 6% during 1973-1984, potentially following changed practice in relation to induction of delivery, and stabilised between 6% and 7% until 1994.

(Figure 2 here)

Characteristics of children born at varying gestational age

Between 1973 and 1994, 4.6% of births were preterm and 9.4% post-term (Table 1). Late preterm children (3.6%) were more likely to have been exposed to maternal medical risk, birth complications, or low Apgar, with highest rates among children born extremely preterm. Moderately post-term children (7.8%) more commonly suffered complicated deliveries or low Apgar, but were less exposed to maternal medical risk. Rates did not change materially for children born exceedingly post-term. Parental age decreased with increasing GA. Birth weight increased with GA to term, but decreased for post-term children.

(Table 1 here)

Grade averages for individuals born at varying gestational age

The grades of children born at appropriate weight-for-GA (AGA) improved with GA towards term (40-41 weeks) and then declined. Irrespective of GA, the grades of SGA children appeared lowest (Figure 3). Knot locations for splines were calculated at 252, 271, 277, 281, 285, 290 and 299 days. Following covariate adjustment (Figure 4), the grades of extremely preterm children (24 weeks 0 days) in three study periods were 0.43 SD (0.38 to 0.49), 0.41 SD (0.36 to 0.46) and 0.32 SD (0.28 to 0.36) below those of full-term counterparts (corresponding with reductions of 21 (19 to 24), 20 (18 to 23) and 16 points (14 to 18) in the post-1998 grading system), suggesting they had improved over time. For extremely post-term children (45 weeks 0 days), grade averages were lower by 0.15 SD (0.13 to 0.17), 0.11 SD (0.08 to 0.15) and 0.12 SD (0.09 to 0.16) across study periods (-8 (-7 to -9), -6 (-4 to -8) and -6 points (-4 to -8)). Models with indicators for SGA and LGA birth (Supplement 6) suggested growth restriction was associated with reduced performance irrespective of GA (-0.13 SD (-0.14 to -0.12) in the most recent study period) and with reduced performance among those born SGA post-term compared with AGA post-term counterparts (-0.12 SD (-0.16 to -0.09) in the most recent study period).

(Figure 3 here)

Associations among matched siblings

Four knots were specified for preterm siblings (252, 271, 277 and 281 days) and three for post-term siblings (285, 290 and 299 days). In matched siblings (Figure 5), effects diminished after adjustment for sibling-averaged GA (darker shading), particularly in the preterm sibling cohort (before: -0.29 SD (-0.34 to 0.24) at 24 weeks, after: -0.18 SD (-0.23 to -0.12) at 24 weeks) and to a lesser extent for post-term siblings (before: -0.11 SD (-0.14 to -0.07) at 45 weeks, after: -0.07 SD (-0.11 to -0.03) at 45 weeks).

(Figure 4 here)

(Figure 5 here)

Sensitivity analyses

Effects of extremely preterm birth (Supplement 4) were stronger in males, or when occurring with congenital anomalies or low Apgar. Post-term effects were stronger when occurring with low Apgar. For births following induction, there was no association between post-term GA and school performance. Importantly, the grades of pre- and post-term children remained lower than those of term counterparts when considering only uncomplicated spontaneous deliveries, with normal Apgar and without congenital anomalies. Additional adjustment for parental educational attainment and welfare benefits resulted in moderately weaker pre- and post-term effects (Supplement 5).

Discussion

This is the first study to detail associations between GA and school performance across the full range of gestation. There were three main findings. First, grade averages were lower for pre- and post-term children than term counterparts although outcomes appeared to improve over time. Second, grades of SGA children were lowest irrespective of GA. Third, despite weaker within-family associations, there were residual pre- and post-term effects among matched siblings.

Strengths and limitations

We used robust statistical methods to assess school performance by GA, examining extremely pre- and post-term births. Exploring familial confounding among matched siblings, our findings allow stronger causal inference with regard to associations between GA and school performance.

We note the following limitations. First, we could not examine children without a grade record (6.3%) limiting the generalisability of our findings to children in mainstream education. Coincidentally, most children with ID, a known correlate of preterm birth^[33], were excluded from analyses (Supplement 2)

which may have led to conservative estimates of preterm effects. Second, for most of the cohort GA was estimated by last menstrual period (LMP) rather than ultrasound. Measurement error in exposure may therefore have resulted in underestimation of population-level^[34] and within-family associations^[35]. Third, the sibling comparison design, while controlling for characteristics that may be missed by covariate-adjustment, is sensitive to bias by sibling non-shared confounding^[35, 36]. In addition to a causal effect on school performance, our findings are therefore consistent with alternative causal scenarios depending on the similarity or dissimilarity of siblings in exposure and confounding characteristics as described by Frisell et al^[35]. Fourth, rates of post-term birth are overestimated when based on LMP^[37, 38]. Given that GA was determined by LMP for most of the cohort (personal communication with Milla Bennis at NBHW), the trends in Figure 2 may exaggerate rates of post-term pregnancy. However, the decline in post-term pregnancy occurred between 1973 and 1984 when GA would still have been routinely assessed with LMP rather than ultrasound. This would suggest other factors, potentially a greater number of induced deliveries, may have influenced rates of post-term pregnancy over time. Fifth, in our sensitivity analyses of the influence of potential causal pathway characteristics, there may have been bias from unmeasured confounders of associations between these potential mediators (e.g. induction of labour, low Apgar, or birth complications) and offspring school performance outcomes. However, our finding of associations where mediators were absent suggests they did not explain the poorer school performance outcomes of children born at early or late GA.

Comparison with previous findings

The improving outcomes of preterm infants over time are in line with Danish evidence of reduction in risk of autism spectrum disorder associated with preterm birth in recent birth cohorts^[39], and may indicate advances in quality of perinatal care. Notwithstanding, the lower grades of SGA children irrespective of GA, suggest an independent effect of fetal growth restriction on later school performance outcomes^[18, 28] which has persisted over time.

Our findings are consistent with previous studies of cognitive and behavioural outcomes for preterm children. Lipkind et al ^[13], Chyi et al ^[20] and MacKay et al ^[11] report increased special educational needs (SEN) and lower maths ^[13, 20], English ^[13] and reading test scores ^[20]. Morse and colleagues ^[19] report greater risk of developmental problems and Larroque et al ^[15, 16] report behavioural problems and increased SEN. In line with a prior Swedish study of matched siblings ^[12], we found residual within-family effects of preterm GA on school performance.

Fewer studies are available to compare findings for post-term children. MacKay et al ^[11] report increased risk of SEN among children born at 42 and 43 weeks. Gunn Eide et al ^[18] report lower IQ among military conscripts born between 42 and 44 weeks and Yang et al ^[22] report lower IQ for children born at 42 and 43 weeks. Our findings extend on this earlier work by showing a modest negative association between post-term GA and school performance controlling for unmeasured familial traits in a matched sibling design.

Finally, our findings for post-term children are consistent with an earlier Danish study which reports increased mortality risk among post-term SGA infants compared with those born post-term at appropriate weight ^[40] and with our previous study on fetal growth which suggests risk for ASD with ID is greatest among SGA infants born post-term ^[41].

Interpretation

Our findings suggest there may be unmeasured familial traits influencing GA at birth and later school performance. Familial confounders of preterm birth and offspring neurodevelopment may involve influences from the shared environment, such as residual socioeconomic factors not captured by our covariates ^[43], or lifestyle factors such as poor diet, smoking during pregnancy ^[44-46], or maternal pre-pregnancy overweight or obesity ^[47-53] in as far as these occurred across pregnancies. A recent study of risk of Attention-Deficit Hyperactivity Disorder in a cohort of matched Swedish siblings suggests familial confounders of preterm birth and offspring neurodevelopment may not be genetic ^[54].

With respect to confounding in post-term effects, maternal pre-pregnancy obesity is known to influence risk of late delivery ^[55-58] and may have confounded associations with offspring neurodevelopment if occurring over multiple pregnancies ^[48-53]. Furthermore, given that the familial risk of prolonged pregnancy may be largely genetic ^[55, 59-61], maternal or fetal genetic factors might confound associations if they also influence offspring neurodevelopment. Two studies using data from the Swedish registers evidence a lesser role for non-genetic familial characteristics in explaining why some pregnancies exceed term ^[62; 55], which may account for the smaller attenuation in effect for post-term siblings in our study.

Residual associations within families suggest there may also be causal links between GA at birth and later school performance. Mechanisms linking preterm birth with poorer performance may involve poor fetal or childhood brain development ^[63, 64] which could precipitate cognitive or behavioural difficulties affecting school performance ^[65-69]. Intrauterine infection, which is associated with prematurity ^[70], may also independently cause problems in fetal brain development and affect school performance ^[71, 72]. Placental deterioration/insufficiency in prolonged gestation may result in fetal anoxia and nutritional deficiencies ^[73, 74], with more or less influence depending on the degree of post-maturity. Meconium aspiration is also common in post-term pregnancy ^[75, 76] and may independently compromise fetal brain development ^[77]. Finally, the less favourable outcomes of post-term SGA infants suggest placental insufficiency may become particularly toxic to neurodevelopment the longer a pregnancy endures.

Conclusions

GA was associated with school performance across the entire range of gestation, with poorer outcomes for children born pre- or post-term and especially for those showing evidence of poor fetal growth. Our findings for matched siblings were consistent with causal effects of pre- and post-term delivery on later school performance, linking birth at early or late GA with modest reductions in grades on leaving secondary education at age 16.

Future directions

Studies are needed to examine these relationships in other populations. Regional differences in management of pre- and post-term pregnancy may help us understand better the variations in policy and practice than could help improve the longer-term cognitive outcomes of children born at non-optimal GA. Future work should also assess whether our findings for post-term children can be replicated for other health outcomes to help inform policies for induction of labour in pregnancies at risk of exceeding term. Modern datasets now tend to base GA on ultrasound rather than the mother's last menstrual period which will reduce measurement error of GA in future studies, thereby lessening bias in the exposure-outcome association. Furthermore, a comparison of models using LMP and ultrasound based GA variables may help to quantify the likely extent of bias in studies where this information was unavailable. Finally, a comparison of outcomes for children born spontaneously at term, induced at term, or allowed to progress post-term may provide useful new information for the management of prolonged pregnancy .

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Contributors: KA, HH, DR and CD conceived the study and HH, KA, RG and DR contributed to its design. SW contributed to the acquisition of data from the Swedish Registers. SW and HH constructed the dataset. HH analysed the data. HH, DR, RE and KA contributed to the interpretation of the results. HH and KA drafted the work for publication and all authors revised it for important intellectual content. EJ provided expert clinical opinion to identify implausible combinations of birth weight and gestational age. Final approval was given by all authors and our contributor. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of interest statement: The authors declare no competing interests.

Acknowledgements: We acknowledge Dr Edward Johnstone for his contribution to this work.

Table 1: Characteristics of children born at varying GA (n=2 008 102)

Gestational age category		<i>Extremely preterm</i>	<i>Very preterm</i>	<i>Preterm</i>	<i>Late preterm</i>	<i>Early term</i>	<i>Full-term</i>	<i>Moderately post-term</i>	<i>Post-term</i>	<i>Very post-term</i>	<i>Extremely post-term</i>
<i>Gestational age in completed weeks</i>		22 – 27	28 – 31	32 – 33	34 – 36	37 – 39	40 – 41	42	43	44	45
<i>Number of individuals</i>		n=1207	n=6746	n=10 358	n=72 998	n=783 409	n=945 693	n=156 467	n=25 171	n=4675	n=1378
<i>Percentage of the sample</i>		0.1 %	0.3 %	0.5 %	3.6 %	39.0 %	47.1 %	7.8 %	1.3 %	0.2 %	0.1 %
		%	%	%	%	%	%	%	%	%	%
Sex	Male	49.5	53.2	55.4	54.4	51.2	50.3	51.8	51.4	50.0	51.4
	Female	50.5	46.8	44.6	45.6	48.8	49.7	48.2	48.6	50.0	48.6
Parity	Primiparous	49.8	50.2	50.9	48.9	39.8	41.8	47.9	50.3	46.9	45.7
	Multiparous	50.2	49.8	49.1	51.1	60.2	58.2	52.1	49.7	53.1	54.4
Apgar score ^A	≤6	56.7	35.1	21.8	8.4	3.2	3.5	5.1	5.9	6.1	5.3
	>6	37.7	60.9	75.3	90.3	96.1	95.9	94.2	93.2	92.7	92.5
	Missing	5.7	4.0	2.9	1.3	0.7	0.6	0.7	0.9	1.3	2.3
Maternal medical risk factors ^B	No	88.7	83.4	85.4	91.4	96.5	98.0	98.5	98.5	98.5	98.6
	Yes	11.0	16.4	14.3	8.5	3.5	2.0	1.5	1.4	1.2	1.3
	Missing	0.3	0.2	0.3	0.2	0.1	0.0	0.1	0.1	0.3	0.2
Maternal psychiatric history ^C	No	81.4	81.9	81.8	83.1	85.7	87.0	86.7	85.6	85.4	82.2
	Yes	18.6	18.1	18.3	17.0	14.3	13.0	13.3	14.4	14.7	17.8
Paternal psychiatric history ^C	No	84.8	84.6	84.6	85.4	87.1	87.6	87.2	86.3	83.9	83.2
	Yes	15.2	15.4	15.4	14.6	12.9	12.4	12.8	13.7	16.1	16.8
Birth complications ^D	No	55.8	43.2	51.3	72.3	81.8	88.1	82.2	79.3	82.3	85.3
	Yes	44.2	56.8	48.7	27.7	18.2	11.9	17.8	20.7	17.8	14.7
Mother's country of birth	Sweden	83.4	87.2	88.2	88.5	88.6	90.3	90.7	90.5	90.8	89.2
	Other	16.7	12.8	11.8	11.5	11.4	9.7	9.3	9.5	9.2	10.8
Father's country of birth	Sweden	84.3	87.0	87.0	88.1	88.2	89.6	90.1	89.6	89.9	88.2
	Other	15.7	13.0	13.0	11.9	11.8	10.4	9.9	10.4	10.1	11.8
Family income in quintiles	1st (lowest)	19.7	18.1	17.7	18.7	21.1	19.5	17.0	14.3	13.3	12.1
	2nd	23.0	18.4	18.3	18.8	20.6	19.8	17.5	14.7	12.5	12.1
	3rd	18.3	21.1	21.2	20.6	20.0	19.7	19.3	17.9	17.5	16.7
	4th	20.6	21.1	21.8	20.9	19.1	19.9	21.6	24.0	25.0	26.9
	5th (highest)	16.3	20.0	19.7	19.8	18.2	20.2	23.6	28.4	31.0	31.5
	Missing	2.1	1.4	1.2	1.2	1.0	0.9	0.9	0.9	0.6	0.7

Table 1, continued

Gestational age category	<i>Extremely preterm</i>	<i>Very preterm</i>	<i>Moderately preterm</i>	<i>Late preterm</i>	<i>Early term</i>	<i>Full-term</i>	<i>Moderately post-term</i>	<i>Post-term</i>	<i>Very post-term</i>	<i>Extremely post-term</i>
<i>Gestational age in completed weeks</i>	22 – 27	28 – 31	32 – 33	34 – 36	37 – 39	40 – 41	42	43	44	45
<i>Number of individuals</i>	n=1207	n=6746	n=10 358	n=72 998	n=783 409	n=945 693	n=156 467	n=25 171	n=4675	n=1378
<i>Percentage of the sample</i>	0.1 %	0.3 %	0.5 %	3.6 %	39.0 %	47.1 %	7.8 %	1.3 %	0.2 %	0.1 %
	mean	mean	mean	mean	mean	mean	mean	mean	mean	mean
Maternal age (in years)	29.1	28.6	28.1	28.1	28.3	28.0	27.6	27.0	26.3	26.3
Paternal age (in years)	32.1	31.3	30.9	30.9	31.1	30.8	30.4	29.9	29.3	29.4
Birth weight (in grams)	973	1512	2060	2742	3394	3675	3803	3766	3713	3654

Notes: (A) Low Apgar was defined as ≤ 6 on any of the 1-, 5-, or 10-minute measurements. (B) Maternal medical risk factors were defined as gestational diabetes and/or (pre-) eclampsia. (C) Parental psychiatric history was defined as a record of in- or out-patient psychiatric care. (D) Birth complications were defined as birth by Caesarean section or assisted delivery.

Figure 1: Selection process for the study cohort

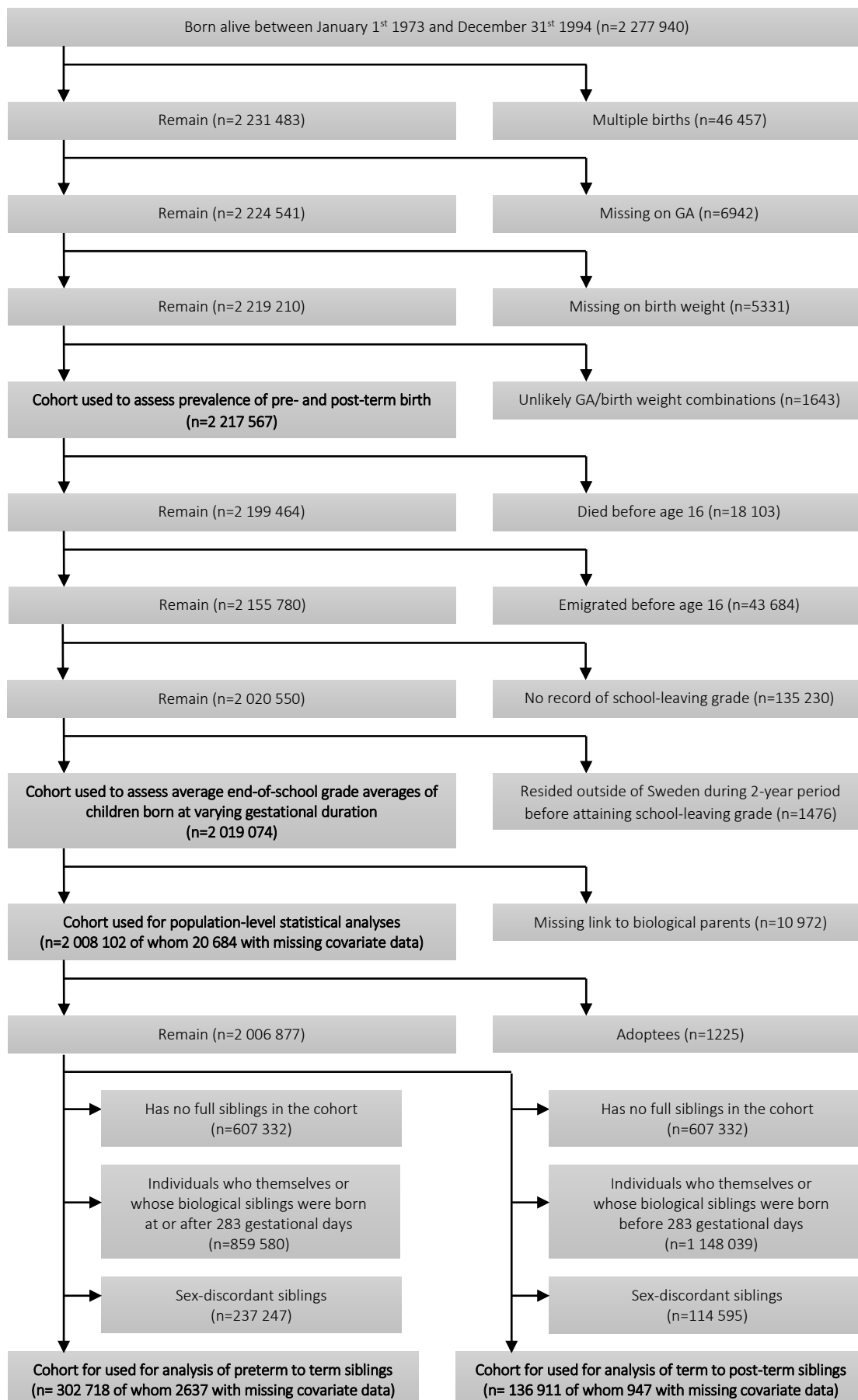
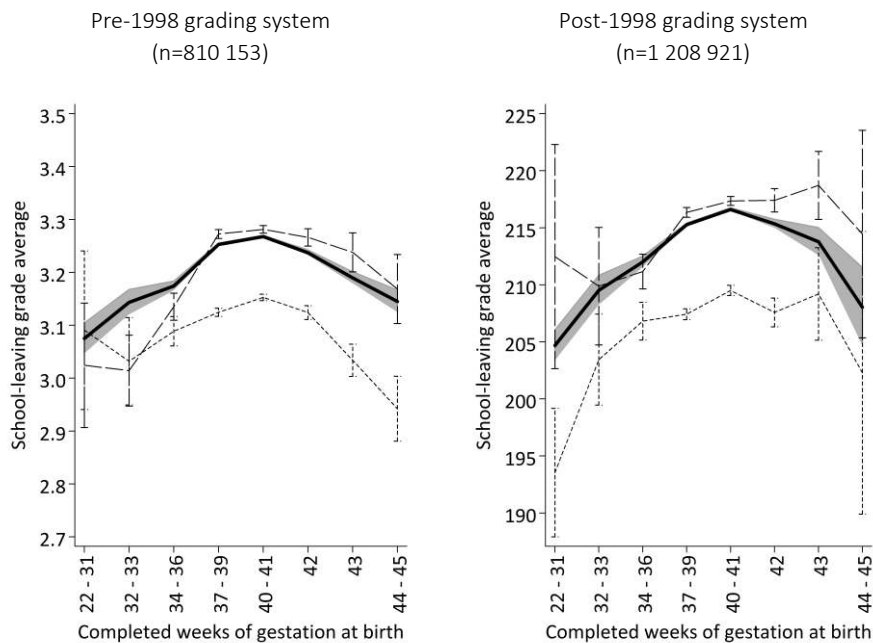


Figure 2: Prevalence of pre- and post-term birth over time (n=2 217 567)

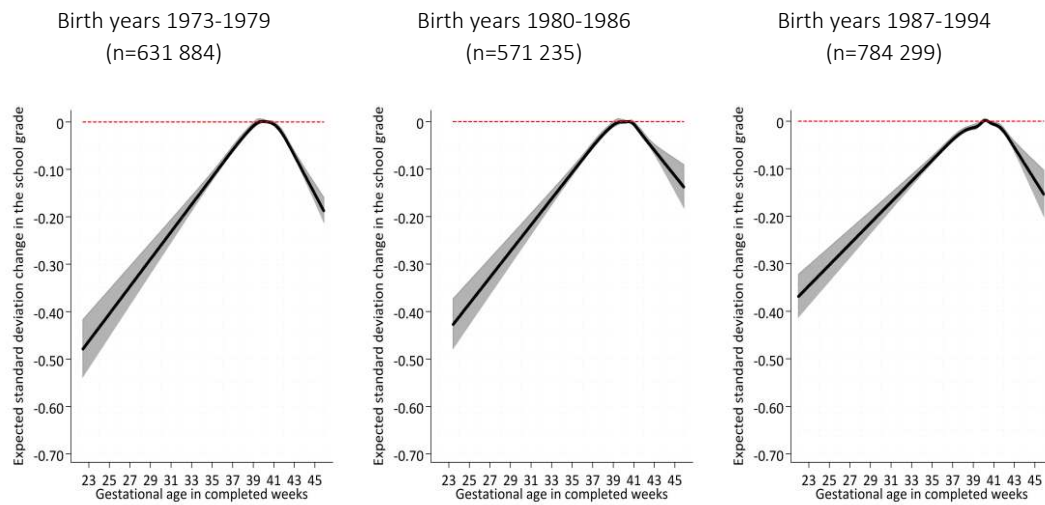


Figure 3: School leaving grade averages of children born at varying gestational duration and small-, appropriate, or large-for-gestational age (n=2 019 074)



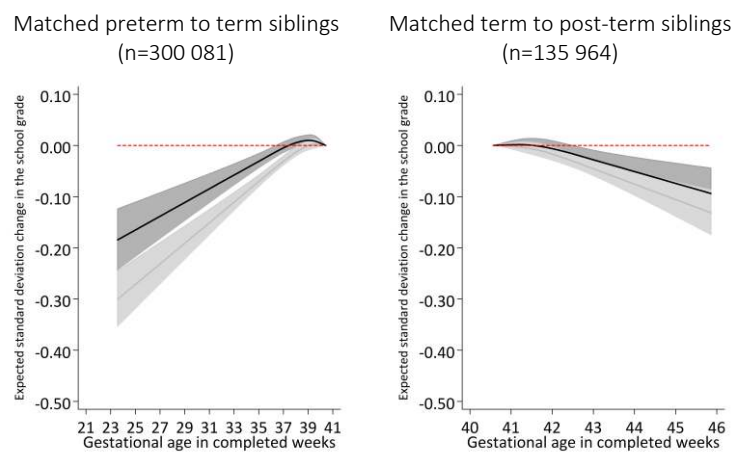
Notes: Solid lines describe school grade averages for individuals born at appropriate weight for gestational age with 95% confidence intervals in gray shading. The short-dotted lines show school grade averages with 95% confidence intervals for individuals born SGA. The long-dashed lines show school grade averages with 95% confidence intervals for individuals born LGA.

Figure 4: Association between age 16 school performance and gestational age at birth in three adjacent study periods (n=1 987 418)



Notes: Curves show the expected standard deviation change in school leaving grade associated with earlier or later GA compared with those born full-term (95% confidence intervals in gray shading). On the horizontal axis, variation in GA is shown by completed weeks to facilitate interpretation. Associations were adjusted for weight-for-gestational age with a quadratic term, birth year, parity, parental age, maternal medical risk factors, parental psychiatric history, parental migration status, family income.

Figure 5 Association between school performance and continuously varying GA at birth among matched siblings (n=1 035 209)



Notes: Curves show the expected standard deviation change in school grade with 95% confidence intervals in gray shading. Associations are shown before (lighter shading) and after (darker shading) adjustment for sibling-averaged GA. On the horizontal axis, variation in GA is shown by completed weeks to facilitate interpretation. Associations were adjusted for weight-for-gestational age including a quadratic term, birth year, parity, parental age, maternal medical risk factors, and family income. Collinearity statistics suggested individual gestational age and sibling-averaged gestational duration were correlated, but not collinear in the preterm to term (VIF: 2.35, condition number: 2.69) and term to post-term sibling cohorts (VIF: 2.13, condition number: 2.52).