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Cause-specific infant mortality in a population-based Swedish study of term and post-term births: the contribution of gestational age and birth weight

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ABSTRACT

Objective: To investigate infant mortality and causes of infant death in relation to gestational age (GA) and birth weight for GA in non-malformed term and post-term infants.

Design: Observational, retrospective nationwide cohort study.

Setting: Sweden 1983–2006.

Participants: 2 152 738 singleton non-malformed infants born at 37 gestational weeks or later.

Main outcome measures: Infant, neonatal and postneonatal mortality and causes of infant death.

Results: Infant mortality rate was 0.12% (n=2687). Compared with infants born at 40 weeks, risk of infant mortality was increased among early term infants (37 weeks, adjusted OR 1.70, 95% CI 1.43 to 2.02). Compared with infants with normal birth weight for GA, very small for gestational age (SGA; <3rd percentile) infants faced a doubled risk of infant mortality (adjusted OR 2.13, 95% CI 1.80 to 2.53), and corresponding risk was also increased among moderately SGA infants (3rd to <10th percentile; adjusted OR 1.46, 95% CI 1.26 to 1.68). Sudden infant death syndrome (SIDS) was the most common cause of death, accounting for 39% of all infant mortality. Compared with birth at 40 weeks, birth at 37 weeks was associated with increased risks of death by infections, cardiovascular disorders, SIDS and malignant neoplasms. Very and moderately SGA were associated with increased risks of death by neonatal respiratory disorders, infections, cardiovascular disorders, SIDS and neuromuscular disorders. High birth weight for GA was associated with increased risks of death by asphyxia and malignant neoplasms.

Conclusion: Early term birth and very to moderately low birth weight for GA are independent risk factors for infant mortality among non-malformed term infants.

ARTICLE SUMMARY

Article focus

- Term infants (born at 37 gestational weeks or more) contribute with 30% to all neonatal mortality. Infants born at 37 and 38 weeks have higher rates of infant mortality than infants born at 40 weeks. Little is known about the interplay between GA and birth weight for GA and its effect on infant mortality.

Key messages

- This study adds detailed analyses of the relationships between GA and birth weight for GA and risks of neonatal and postneonatal mortality and causes of infant death. We conclude that induced deliveries before 39 weeks gestation should be avoided when possible and that extra caution should be taken in term pregnancies with suspected severe or moderate intrauterine growth restriction.

Strengths and limitations of this study

- The main strengths of this study are related to sample size and to the large number of predefined risk factors and confounders. Limitations were that some malformations may not have been detected, causing a theoretical selection bias, and that time trends may have influenced the outcome.

INTRODUCTION

In studies of gestational age (GA) and risks of infant mortality and morbidity, infants born at term (ie, at 37–41 weeks) are commonly used as a reference group. However, recent studies highlight that compared with infants born at 40 weeks, infants born at 37 and 38 weeks have higher rates of infant, neonatal and postneonatal mortality, as well as neonatal morbidity.[1 2] Term infants contribute approximately 30% of all infant mortality.[3] Low birth weight may be a result

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of short GA and/or restricted fetal growth and infants born small for gestational age (SGA) are at increased risk of infant mortality. In a study of more than 300 000 infants, both late preterm (34–36 weeks) and term born SGA infants were at increased risk of infant mortality compared with infants with a normal birth weight for GA. Almost half of infant mortality among these infants was caused by congenital conditions, but SGA infants were also at increased risk of infant mortality after excluding infant deaths caused by congenital anomalies.[4]

To our knowledge, there are no previous studies on how GA interacts with birth weight for GA on risks of neonatal and postneonatal mortality or causes of infant death in term and post-term infants. Moreover, earlier studies have not separated neonatal and postneonatal mortality or compared risks of mortality or causes of infant deaths in term and post-term infants. In addition, information about possible confounders was also limited in previous studies.

In the present nationwide Swedish investigation, we have included information on maternal and infant characteristics on more than 2 million singleton live births. The aims of this study are to clarify the associations between GA and birth weight for GA and risks of infant, neonatal and postneonatal mortality as well as causes of infant death in term and post-term born non-malformed infants.

METHODS

Data sources

The Swedish National Board of Health and Welfare and Statistics Sweden provided data from four population-based registers. Record linkage of individuals across these registries was made possible through the unique National Registration Number assigned to each Swedish resident at birth or immigration.[5] The Swedish Birth Register started in 1973 and contains prospectively collected data on the mother, pregnancy, delivery and infant on 98%–99% of all births in Sweden.[6 7] The Education Register includes information on highest level of formal education level and is updated yearly. The Cause of Death Register collects data on date and cause of death on all Swedish residents. The Register of Population and Population Changes holds information on dates of birth, death, immigration and emigration of all Swedish residents. The study protocol was approved by the regional ethical vetting board at Karolinska Institutet.

Study population

The study population was defined as all live singleton infants with information on birth weight and GA, born at 37 completed gestational weeks or later and registered in the Birth Registry in 1983–2006 (n=2 242 591). In the Birth and Cause of Death Registers, diagnoses and causes of death are coded according to the International Classification of Diseases (ICD). The eighth revision (ICD-8) was used from 1983 to 1986, ICD-9 was used from 1987 to 1996 and ICD-10 was used from 1997 to 2006. We excluded infants with a malformation diagnosis (ICD-8: 740–759, ICD-9: 740–759 or ICD-10: Q00–Q99) in the Birth Registry and/or the Cause of Death Registry (n=89 853). The final study population included 2 152 738 infants.

Exposures

Our two main exposures were GA and birth weight for GA. Estimation of GA was made by ultrasound around the 17th week of gestation. If no early second trimester ultrasound scan was available, last menstrual period was used to calculate GA. Birth weight for GA was categorised into percentiles of expected birth weight for GA according to the Swedish reference curve for normal fetal growth (3rd, 10th, 25th, 75th, 90th and 97th percentiles).[8] At the first antenatal visit (usually at 8–12 gestational weeks), women were interviewed on their smoking habits (non-smoker, 1–9 cigarettes daily and 10 or more cigarettes daily) and health status, and the data were forwarded to the Birth Registry. At delivery, information on the mother's age and parity, diagnoses (pre-eclampsia, premature rupture of membranes, hypertension and diabetes), mode of delivery (cesarean, vaginal instrumental and vaginal non-instrumental delivery), infant's year of birth, birth weight, sex, GA and diagnoses at discharge was collected and forwarded to the Birth Register. Information on mother's education level was obtained from the Education Registry in 2005 and was categorised into 9 years or less, 10–11 years, 12 years, 13–14 years and 15 years or more. Largely, this categorisation corresponds with Swedish compulsory education (7–16 years of age), vocational secondary education, pre-academic secondary education, college and university-level studies. Information on the mother's country of birth (Sweden, other Nordic countries (Denmark, Finland, Iceland and Norway) and outside the Nordic countries) was provided by the Register of Population and Population Changes.

Outcome

Outcome was defined by information on time or cause of death, provided by the Cause of Death Registry. Infant mortality was defined as death of a live born infant during the first year of life (0–364 completed days of age). Infant mortality was categorised into neonatal mortality, defined as death at 0–27 completed days of age, and postneonatal mortality, defined as death at 28–364 completed days of age. Cause of death was categorised into nine groups according to the following ICD codes: asphyxia (ICD-8: 77640–77650, 76840, 76890; ICD-9: 768; ICD-10: P20–P21), neonatal respiratory disorders (ICD-8: 77600–77629, 77660; ICD-9: 769–770, 786; ICD-10: P22, P24), infections (ICD-8: 000–139, 320–324, 460–486, 590; ICD-9: 000–139, 320–324, 464–466, 480–499, 590, 770–771; ICD-10: A01–A99, B01–B99, G00–G09, J02–J22, P23, P35–P39), cardiovascular disorders (ICD-8/ICD-9:

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391–459; ICD-10: I00–I99, P29, P91), sudden infant death syndrome (SIDS; ICD-8: 79500; ICD-9: 798; ICD-10: R95), neuromuscular disorders (ICD-8/ICD-9: 330–359; ICD-10: G10–G99), malignant neoplasms (ICD-8/ICD-9: 140–209; ICD-10: C00–C99), external causes of death (ICD-8/ICD-9: 800–999; ICD-10: V00–V99, W00–W99, Y00–Y99, X00–X99) and other (remaining) causes of death.

Statistical analyses

Stratum-specific death rates were calculated as ((number of deaths in the stratum)/(number of infants at risk in the stratum)). Outcome was stratified by GA at birth and birth weight for GA. Crude and adjusted ORs were calculated by logistic regression. In the first model, we adjusted for year of birth, and GA was adjusted for birth weight for GA and vice versa. In the second adjusted model, we also adjusted for mother's country of birth, education level, age, parity, smoking status in early pregnancy, pre-eclampsia, premature rupture of membranes, diagnosis of pregestational and/or gestational hypertension or diabetes, mode of delivery, year of delivery and infant's sex. Infants who were born at 40 gestational weeks and/or with normal birth weight for GA (within the 25th to 75th percentiles) served as reference group. In analyses of postneonatal mortality, we included infants alive at 28 days of age. Birth weight for GA was a priori considered a possible effect-modifier on the association of GA and infant, neonatal and postneonatal mortality. Effect modification was tested by likelihood ratio interaction test and stratification.

RESULTS

Of the total 2 152 738 infants born at 37 completed weeks or later, 2687 (0.12%) infants died during the first year of life. There were 882 (0.04%) neonatal deaths and 1805 (0.08%) postneonatal deaths. The infant mortality rate/1000 live births was 2.37 among infants born at 37 weeks, 1.52 at 38 weeks, 1.18 at 39 weeks, 1.08 at 40 weeks, 1.13 at 41 weeks and 1.30 at 42 weeks or more. The distribution of risk factors among survivors and non-survivors at 1 year of age is presented in eTable 1.

Infant mortality

Compared with infants born at 40 weeks, infants born at 37 gestational weeks had a more than doubled risk of infant mortality in crude analyses. After adjustment for maternal, pregnancy and infant factors, being born at 37 weeks was associated with a 70% increased risk of infant mortality. Compared with infants with normal birth weight for GA, infants who were assessed as very small for GA (very SGA; <3rd percentile) had a doubled infant mortality risk and moderately small for GA infants (moderately SGA; between the 3rd and the 10th percentiles) had a 50% increased risk in the fully adjusted model (table 1).

Neonatal mortality

Compared with infants born at 40 weeks, infants born at 37 weeks were at a 2.6-fold increased risk of neonatal mortality in the crude analysis and a 70% increased risk in the fully adjusted analysis. Post-term infants had a 70% increased risk of neonatal mortality in the crude analysis and a 40% increased risk in the fully adjusted

Table 1 Risk of infant mortality in non-malformed singleton term infants born 1983–2006, by gestational week at birth and birth weight for gestational age (GA) (n=2 152 738)

	Infant mortality				
	Live births (n)	Deaths (n)	Crude (n=2687) OR (95% CI)	Adjusted model 1* (n=2687) OR (95% CI)	Adjusted model 2† (n=2177) OR (95% CI)
Gestational week					
37	98 326	233	2.20 (1.90 to 2.56)	2.16 (1.86 to 2.51)	1.70 (1.43 to 2.02)
38	241 277	368	1.42 (1.25 to 1.61)	1.42 (1.25 to 1.62)	1.15 (1.00 to 1.34)
39	448 264	530	1.10 (0.98 to 1.23)	1.10 (0.98 to 1.23)	1.05 (0.92 to 1.19)
40	595 569	642	1.00 (Reference)	1.00 ((Reference)	1.00 (Reference)
41	451 257	511	1.05 (0.94 to 1.18)	1.04 (0.93 to 1.17)	1.03 (0.91 to 1.18)
42+	310 806	403	1.20 (1.06 to 1.36)	1.15 (1.01 to 1.30)	1.07 (0.93 to 1.23)
Birth weight for GA percentiles					
<3	62 635	202	2.82 (2.43 to 3.27)	2.59 (2.23 to 3.01)	2.13 (1.80 to 2.53)
3–<10	151 558	280	1.61 (1.41 to 1.83)	1.58 (1.38 to 1.79)	1.46 (1.26 to 1.68)
10–<25	321 184	409	1.11 (0.99 to 1.24)	1.10 (0.98 to 1.23)	1.08 (0.95 to 1.22)
25–75	1 074 943	1234	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
>75–90	321 668	336	0.91 (0.81 to 1.03)	0.91 (0.80 to 1.02)	0.87 (0.76 to 1.00)
>90 to 97	150 183	146	0.85 (0.71 to 1.01)	0.85 (0.71 to 1.00)	0.79 (0.65 to 0.96)
>97	63 328	80	1.10 (0.88 to 1.38)	1.08 (0.86 to 1.36)	1.06 (0.84 to 1.36)

*Model 1 adjusts for year of birth and birth weight percentiles or gestational week.
†Model 2 additionally adjusts for mother's country of birth, education level, age, parity, smoking status in early pregnancy, pre-eclampsia, premature rupture of membranes, diagnosis of hypertension or diabetes, mode of delivery, year of delivery and infant's sex.

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Table 2 Risk of neonatal mortality in non-malformed singleton term infants born 1983–2006, by gestational week at birth and birth weight for gestational age (GA) (n=2 152 738)

	Neonatal mortality				
	Live births (n)	Deaths (n)	Crude (n=882) OR (95% CI)	Adjusted model 1* (n=882) OR (95% CI)	Adjusted model 2† (n=705) OR (95% CI)
Gestational week					
37	98 326	86	2.62 (2.03 to 3.37)	2.49 (1.93 to 3.21)	1.73 (1.29 to 2.31)
38	241 277	103	1.28 (1.01 to 1.62)	1.26 (0.99 to 1.60)	0.86 (0.65 to 1.13)
39	448 264	133	0.89 (0.71 to 1.11)	0.89 (0.71 to 1.10)	0.84 (0.66 to 1.08)
40	595 569	199	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
41	451 257	186	1.23 (1.01 to 1.51)	1.22 (1.00 to 1.49)	1.20 (0.96 to 1.50)
42+	310 806	175	1.69 (1.38 to 2.07)	1.59 (1.30 to 1.95)	1.36 (1.08 to 1.71)
Birth weight for GA percentile					
<3	62 635	81	3.51 (2.76 to 1.40)	3.23 (2.54 to 4.10)	2.54 (1.93 to 3.33)
3–<10	151 558	98	1.75 (1.40 to 2.19)	1.69 (1.35 to 2.11)	1.58 (1.23 to 2.02)
10 to <25	321 184	119	1.00 (0.82 to 1.23)	0.99 (0.81 to 1.21)	1.01 (0.81 to 1.27)
25–75	1 074 943	397	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
>75–90	321 668	95	0.80 (0.64 to 1.00)	0.81 (0.64 to 1.01)	0.74 (0.57 to 0.95)
>90–97	150 183	58	1.05 (0.79 to 1.38)	1.05 (0.80 to 1.38)	0.91 (0.66 to 1.25)
>97	63 328	34	1.45 (1.02 to 2.06)	1.44 (1.01 to 2.04)	1.36 (0.93 to 1.98)

*Model 1 adjusts for year of birth and birth weight percentiles or gestational week.
†Model 2 additionally adjusts for mother's country of birth, education level, age, parity, smoking status in early pregnancy, pre-eclampsia, premature rupture of membranes, diagnosis of hypertension or diabetes, mode of delivery, year of delivery and infant's sex.

analysis. Compared with normal birth weight infants, very SGA infants had a 2.5-fold increased risk and moderately SGA infants a more than 50% increased risk of neonatal mortality in the fully adjusted model (table 2).

Postneonatal mortality

Compared with infants born at 40 weeks, infants born at 37 weeks had a doubled risk of postneonatal mortality in the crude analysis and a 70% increased risk in the fully adjusted analysis. Infants born at 38 weeks also had an increased risk of postneonatal mortality. Compared with infants with normal birth weight for GA, very SGA infants had an almost doubled risk and moderately SGA infants a 40% increased risk of postneonatal mortality in the fully adjusted model (table 3). We did not detect any interactions between GA and birth weight for GA on the

Table 3 Risk of postneonatal mortality (28–364 days) in non-malformed singleton term infants born 1983–2006 and alive at 28 days of age, by gestational week at birth and birth weight for gestational age (GA) (n=2 151 746)

	Postneonatal mortality				
	Alive at 28 days (n)	Deaths (n)	Crude (n=1805) OR (95% CI)	Adjusted model 1* (n=1805) OR (95% CI)	Adjusted model 2† (n=1472) OR (95% CI)
Gestational week					
37	98 240	147	2.01 (1.67 to 2.43)	2.00 (1.66 to 2.41)	1.68 (1.36 to 2.10)
38	241 174	265	1.48 (1.27 to 1.72)	1.50 (1.29 to 1.74)	1.34 (1.12 to 1.59)
39	448 131	397	1.19 (1.04 to 1.36)	1.20 (1.05 to 1.37)	1.15 (0.99 to 1.33)
40	595 310	443	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
41	451 071	325	0.97 (0.84 to 1.12)	0.96 (0.84 to 1.11)	0.96 (0.82 to 1.12)
42+	310 631	228	0.99 (0.84 to 1.16)	0.95 (0.81 to 1.11)	0.92 (0.77 to 1.10)
Birth weight for GA percentile					
<3	62 554	121	2.49 (2.05 to 3.01)	2.29 (1.89 to 2.78)	1.92 (1.53 to 2.41)
3 to <10	151 460	182	1.54 (1.31 to 1.81)	1.51 (1.29 to 1.77)	1.40 (1.17 to 1.68)
10–<25	321 065	290	1.16 (1.02 to 1.33)	1.15 (1.01 to 1.31)	1.11 (0.95 to 1.29)
25–75	1 074 546	837	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
>75–90	321 573	241	0.96 (0.83 to 1.11)	0.96 (0.83 to 1.11)	0.94 (0.80 to 1.10)
>90–97	150 125	88	0.75 (0.60 to 0.94)	0.75 (0.60 to 0.94)	0.74 (0.58 to 0.94)
>97	63 294	46	0.93 (0.69 to 1.26)	0.92 (0.68 to 1.23)	0.92 (0.67 to 1.27)

*Model 1 adjusts for year of birth and birth weight percentiles or gestational week.
†Model 2 additionally adjusts for mother's country of birth, education level, age, parity, smoking status in early pregnancy, pre-eclampsia, premature rupture of membranes, diagnosis of hypertension or diabetes, mode of delivery, year of delivery and infant's sex.
GA, Gestational Age.

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risk of infant, neonatal or postneonatal mortality. Observations with missing data on any risk factor were excluded from the fully adjusted models. We did not detect any significant difference of results when comparing analysis before and after exclusion of missing data.

Cause of death

The main causes of infant death were asphyxia (9.9%), neonatal respiratory disorders (3.6%), infections (11.3%), cardiovascular disorders (3.4%), SIDS (39.5%), neuromuscular disorders (5.3%), malignant neoplasms (2.0%), external causes (3.5%) and other causes (22.3%). In the 'other causes' category, three subcategories (neonatal morbidity except respiratory diseases and infections, birth trauma and metabolic diseases) accounted for two-thirds of the mortality.

Table 4 shows GA and birth weight for GA and risks of infant mortality by cause. Compared with infants born at 40 weeks, infants born at early term age were at increased risks of death by infections (a more than threefold risk at 37 weeks and a more than twofold risk at 38 weeks), cardiovascular disorders (an almost threefold risk at 37 weeks), SIDS (an almost twofold risk at 37 weeks and an almost 50% risk increase at 38 weeks), malignant neoplasms (a more than threefold risk at 37 weeks) and other causes of death (an almost threefold risk at 37 weeks). Infants born at 41 weeks or post-term (≥42 weeks) infants were at increased risk of death by asphyxia (a 50% risk increase at 41 weeks and a 2.5-fold risk increase at ≥42 weeks), neonatal respiratory disorders (a doubled risk at ≥42 weeks) and infections (a 50% risk increase at ≥42 weeks). Compared with infants with normal birth weight for GA (25th to 75th percentiles), very SGA infants (<3rd percentile) had more than fourfold increased risks of death by neonatal respiratory disorders and cardiovascular disorders, more than tripled risks of deaths by neuromuscular disorders and other causes of death, and more than doubled risks of deaths by infections and SIDS. For moderately SGA infants (3rd to 10th percentiles), risks of death by neonatal respiratory disorders and other causes of death were more than doubled and risk of SIDS was increased by 40%. Infants who were very large for GA (very LGA; above the 97th percentile) had more than a tripled increase in risk of death by asphyxia and malignant neoplasms. Infants with a modestly increased birth weight for GA (75th to 90th percentiles) had a doubled risk of death by neoplasms.

DISCUSSION

In this nationwide population-based study, we found that the increased all-cause infant mortality risk among early term (37 weeks) non-malformed infants was due to increased risks of death by infections, cardiovascular diseases, SIDS and malignant neoplasms. Being born very SGA (<3rd percentile) was associated with a more than doubled risk, and being born moderately SGA (3rd to 10th percentiles) was associated with an almost 50% increased risk of infant mortality. Low birth weight for GA was associated with increased risks of death by all causes except malignant diseases. Post-term birth (42 + weeks) was a risk factor for neonatal but not for post-neonatal mortality and was associated with increased risks of death by infections, neonatal respiratory disorders and asphyxia. High birth weight for GA was associated with increased risks of death by asphyxia and malignant diseases. This is the first study to show the interplay between GA and birth weight for GA with respect to risks of neonatal and postneonatal mortality and causes of infant death in term, non-malformed infants. Access to a large database permitted the inclusion of a wide range of possible confounders and enabled the separation of infant mortality into neonatal and postneonatal mortality. Additionally, an analysis of the contribution of GA and birth weight for GA to cause of death in term and post-term infants was performed.

Strengths and limitations

The main strengths of our study were related to sample size and precision but also to the large number of predefined risk factors and confounders. GA was determined by ultrasound in most pregnancies, data were prospectively recorded and the number of pregnancies with missing information was low. The validity of self-reported smoking has been reported to be high among pregnant women in the Swedish Birth Registry.[9] However, one limitation was that some malformations may not have been detected and diagnosed at the physical examination after birth. As all malformation-related death causes were excluded from the study, the majority of these undetected malformations would probably not be related to infant mortality. However, the remaining malformations in the study group could be a theoretical source of selection bias. In addition, sample size was not large enough to adjust analyses of causes of death for all confounders. Time trends may also have influenced the outcome, as obstetric and neonatal care as well as diagnostic practices and rates of infant mortality have changed during the study period. We have tried to control for this time effect by adjusting all analyses for year of birth.

GA and infant mortality

Infant mortality is inversely related to GA at birth, and this association persists even at late preterm and term gestations.[2 10 11] This fact may not be publicly recognised and the heterogeneity of risk within the group of term infants deserves more attention. Data on risks of infant, neonatal and postneonatal mortality in different gestational weeks and identification of especially vulnerable individuals are necessary when planning elective deliveries and for assembling the right competence and surveillance around the newborn infant after delivery.[10] There has been a tendency to electively deliver infants on relative indications at early term GAs in Western countries, instead of postponing delivery until the pregnancy has reached full term. As demonstrated

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Table 4 Cause of death by gestational week at birth and birth weight for GA percentile among term, non-malformed infants

Gestational week or birth weight for GA percentile	Infant mortality			
	Mortality number	Rate/1000 live births	Crude OR (95% CI)	Adjusted model 1 OR (95% CI)
Asphyxia (n=238)				
37	12	0.12	1.43 (0.76 to 2.67)	1.36 (0.72 to 2.55)
38	14	0.06	0.68 (0.38 to 1.22)	0.66 (0.37 to 1.19)
39	31	0.07	0.81 (0.52 to 1.26)	0.80 (0.51 to 1.25)
40	51	0.09	1.00 (Reference)	1.00 (Reference)
41	61	0.14	1.58 (1.09 to 2.29)	1.58 (1.10 to 2.29)
≥42	69	0.22	2.59 (1.81 to 3.72)	2.58 (1.79 to 3.71)
<3	10	0.73	1.53 (0.80 to 2.93)	1.47 (0.77 to 2.80)
3–<10	23	0.15	1.46 (0.93 to 2.28)	1.39 (0.89 to 2.18)
10–<25	29	0.09	0.87 (0.58 to 1.30)	0.84 (0.56 to 1.27)
25–75	112	0.10	1.00 (Reference)	1.00 (Reference)
>75–90	29	0.09	0.87 (0.58 to 1.30)	0.89 (0.59 to 1.33)
>90–97	16	0.11	1.02 (0.61 to 1.73)	1.06 (0.63 to 1.79)
>97	19	0.30	2.88 (1.77 to 4.69)	3.09 (1.89 to 5.03)
Neonatal respiratory disorders (n=87)				
37	5	0.05	1.38 (0.52 to 3.64)	1.33 (0.50 to 3.53)
38	7	0.03	0.79 (0.34 to 1.84)	0.80 (0.34 to 1.88)
39	6	0.01	0.36 (0.15 to 0.89)	0.37 (0.15 to 0.91)
40	22	0.04	1.00 (Reference)	1.00 (Reference)
41	22	0.05	1.32 (0.73 to 2.38)	1.28 (0.71 to 2.31)
≥42	25	0.08	2.18 (1.23 to 3.86)	1.92 (1.08 to 3.42)
<3	11	0.37	4.61 (2.37 to 8.96)	4.10 (2.10 to 8.01)
3–<10	16	0.11	2.77 (1.55 to 4.93)	2.55 (1.43 to 4.54)
10–<25	12	0.04	0.98 (0.52 to 1.86)	0.94 (0.49 to 1.78)
25–75	41	0.04	1.00 (Reference)	1.00 (Reference)
>75–90	2	0.01	0.16 (0.04 to 0.67)	0.17 (0.04 to 0.70)
>90–97	5	0.03	0.87 (0.35 to 2.21)	0.92 (0.36 to 2.34)
>97	0	0	–	–
Infections (n=317)				
37	35	0.36	3.37 (2.23 to 5.09)	3.34 (2.21 to 5.05)
38	55	0.23	2.16 (1.50 to 3.09)	2.18 (1.52 to 3.14)
39	51	0.11	1.08 (0.74 to 1.56)	1.08 (0.75 to 1.56)
40	63	0.11	1.00 (Reference)	1.00 (Reference)
41	62	0.14	1.30 (0.92 to 1.84)	1.29 (0.91 to 1.84)
≥42	51	0.16	1.55 (1.07 to 2.24)	1.49 (1.03 to 2.16)
<3	25	0.39	2.67 (1.75 to 4.06)	2.39 (1.57 to 3.65)
3–<10	27	0.18	1.19 (0.79 to 1.79)	1.15 (0.77 to 1.74)
10–<25	43	0.13	0.89 (0.64 to 1.25)	0.89 (0.63 to 1.24)
25–75	161	0.15	1.00 (Reference)	1.00 (Reference)
>75–90	34	0.11	0.71 (0.49 to 1.02)	0.70 (0.49 to 1.02)
>90–97	21	0.14	0.93 (0.59 to 1.47)	0.92 (0.58 to 1.45)
>97	6	0.09	0.63 (0.28 to 1.43)	0.60 (0.27 to 1.36)
Cardiovascular disorders (n=95)				
37	10	0.10	2.89 (1.36 to 6.13)	2.80 (1.32 to 5.96)
38	9	0.04	1.06 (0.49 to 2.31)	1.07 (0.49 to 2.34)
39	23	0.05	1.46 (0.81 to 2.63)	1.47 (0.81 to 2.65)
40	21	0.04	1.00 (Reference)	1.00 (Reference)
41	15	0.03	0.94 (0.49 to 1.83)	0.92 (0.48 to 1.79)
≥42	17	0.05	1.55 (0.82 to 2.94)	1.42 (0.75 to 2.70)
<3	11	0.17	4.50 (2.32 to 8.73)	4.21 (2.16 to 8.20)
3–<10	10	0.07	1.69 (0.85 to 3.37)	1.67 (0.84 to 3.34)
10–<25	16	0.05	1.28 (0.72 to 2.27)	1.27 (0.72 to 2.27)

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Table 4 Continued

Gestational week or birth weight for GA percentile	Infant mortality		Crude OR (95% CI)	Adjusted model 1 OR (95% CI)
	Mortality number	Rate/1000 live births		
25–75	42	0.04	1.00 (Reference)	1.00 (Reference)
>75–90	10	0.03	0.80 (0.40 to 1.59)	0.79 (0.40 to 1.58)
>90–97	5	0.03	0.85 (0.34 to 2.15)	0.84 (0.33 to 2.12
>97	1	0.02	0.40 (0.06 to 2.94)	0.39 (0.05 to 2.81)
SIDS (n=1107)				
37	90	0.92	1.87 (1.48 to 2.37)	1.86 (1.47 to 2.35)
38	171	0.71	1.45 (1.20 to 1.75)	1.47 (1.21 to 1.77)
39	235	0.52	1.07 (0.90 to 1.27)	1.07 (0.91 to 1.28)
40	292	0.49	1.00 (Reference)	1.00 (Reference)
41	194	0.43	0.88 (0.73 to 1.05)	0.87 (0.73 to 1.05)
≥42	125	0.40	0.82 (0.67 to 1.01)	0.79 (0.64 to 0.97)
<3	79	1.22	2.61 (2.06 to 3.31)	2.40 (1.89 to 3.04)
3–<10	107	0.71	1.46 (1.19 to 1.80)	1.43 (1.16 to 1.76)
10–<25	178	0.55	1.15 (0.97 to 1.36)	1.14 (0.96 to 1.35)
25–75	519	0.48	1.00 (Reference)	1.00 (Reference)
>75–90	147	0.46	0.95 (0.79 to 1.14)	0.95 (0.79 to 1.14)
>90–97	51	0.34	0.70 (0.53 to 0.94)	0.70 (0.53 to 0.94)
>97	26	0.41	0.85 (0.57 to 1.26)	0.84 (0.57 to 1.24)
Neuromuscular disorders (n=143)				
37	9	0.09	1.65 (0.79 to 3.45)	1.61 (0.77 to 3.36)
38	18	0.07	1.35 (0.76 to 2.39)	1.36 (0.76 to 2.41)
39	33	0.07	1.33 (0.82 to 2.15)	1.34 (0.83 to 2.17)
40	33	0.06	1.00 (Reference)	1.00 (Reference)
41	31	0.07	1.24 (0.76 to 2.02)	1.22 (0.75 to 1.99)
≥42	19	0.06	1.10 (0.63 to 1.94)	1.02 (0.58 to 1.80)
<3	15	0.31	3.84 (2.20 to 6.73)	3.72 (2.12 to 6.53)
3–<10	13	0.09	1.38 (0.76 to 2.49)	1.37 (0.75 to 2.48)
10–<25	26	0.08	1.30 (0.83 to 2.04)	1.30 (0.82 to 2.04)
25–75	67	0.06	1.00 (Reference)	1.00 (Reference)
>75–90	16	0.05	0.80 (0.46 to 1.38)	0.80 (0.46 to 1.38)
>90–97	3	0.02	0.32 (0.10 to 1.02)	0.32 (0.10 to 1.02)
>97	3	0.05	0.76 (0.24 to 2.42)	0.75 (0.24 to 2.40)
Malignant neoplasms (n=56)				
37	5	0.05	3.37 (1.13 to 10.05)	3.26 (1.09 to 9.75)
38	7	0.03	1.92 (0.72 to 5.16)	1.85 (0.69 to 4.98)
39	17	0.04	2.51 (1.12 to 5.63)	2.46 (1.10 to 5.53)
40	9	0.02	1.00 (Reference)	1.00 (Reference)
41	9	0.02	1.32 (0.52 to 3.33)	1.36 (0.54 to 3.43)
≥42	9	0.03	1.92 (0.76 to 4.83)	2.05 (0.81 to 5.16)
<3	0	0	–	–
3–<10	4	0.03	1.23 (0.43 to 3.57)	1.19 (0.41 to 3.45)
10–<25	6	0.02	0.87 (0.36 to 2.14)	0.86 (0.35 to 2.12)
25–75	23	0.02	1.00 (Reference)	1.00 (Reference)
>75–90	14	0.04	2.03 (1.05 to 3.95)	2.03 (1.05 to 3.95)
>90–97	4	0.03	1.25 (0.43 to 3.60)	1.23 (0.43 to 3.57)
>97	5	0.08	3.69 (1.40 to 9.71)	3.58 (1.36 to 9.46)
External causes of death (n=96)				
37	6	0.06	1.58 (0.64 to 3.88)	1.56 (0.63 to 3.83)
38	13	0.05	1.40 (0.71 to 2.75)	1.40 (0.71 to 2.78)
39	24	0.05	1.39 (0.78 to 2.46)	1.39 (0.79 to 2.46)
40	23	0.04	1.00 (Reference)	1.00 (Reference)
41	18	0.04	1.03 (0.56 to 1.91)	1.03 (0.56 to 1.91)
≥42	12	0.04	1.00 (0.50 to 2.01)	0.97 (0.48 to 1.95)

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Table 4 Continued

Gestational week or birth weight for GA percentile	Infant mortality		Crude OR (95% CI)	Adjusted model 1 OR (95% CI)
	Mortality number	Rate/1000 live births		
<3	6	0.11	2.19 (0.94 to 5.13)	2.10 (0.90 to 4.92)
3–<10	9	0.06	1.36 (0.67 to 2.77)	1.35 (0.66 to 2.75)
10–<25	14	0.04	1.00 (0.55 to 1.81)	0.99 (0.55 to 1.81)
25–75	47	0.04	1.00 (Reference)	1.00 (Reference)
>75–90	14	0.04	1.00 (0.55 to 1.81)	0.99 (0.55 to 1.80)
>90–97	2	0.01	0.31 (0.07 to 1.25)	0.30 (0.07 to 1.25)
>97	4	0.06	1.45 (0.52 to 4.01)	1.42 (0.51 to 3.95)
Other causes of death (n=568)				
37	62	0.63	2.87 (2.12 to 3.88)	2.75 (2.03 to 3.72)
38	78	0.32	1.47 (1.11 to 1.95)	1.45 (1.10 to 1.92)
39	112	0.25	1.14 (0.88 to 1.46)	1.14 (0.88 to 1.46)
40	131	0.22	1.00 (Reference)	1.00 (Reference)
41	106	0.23	1.07 (0.83 to 1.38)	1.06 (0.82 to 1.36)
≥42	79	0.25	1.16 (0.87 to 1.53)	1.08 (0.82 to 1.43)
<3	48	1.55	3.59 (2.63 to 4.89)	3.30 (2.41 to 4.50)
3–<10	74	0.49	2.28 (1.76 to 2.97)	2.23 (1.71 to 2.90)
10–<25	90	0.28	1.31 (1.03 to 1.67)	1.30 (1.02 to 1.66)
25–75	230	0.21	1.00 (Reference)	1.00 (Reference)
>75–90	71	0.22	1.03 (0.79 to 1.35)	1.03 (0.79 to 1.35)
>90–97	39	0.26	1.21 (0.86 to 1.70)	1.20 (0.85 to 1.69)
>97	16	0.25	1.18 (0.71 to 1.96)	1.13 (0.68 to 1.88)

Model 1 adjusts for year of birth and birth weight SD percentile or gestational week.
SIDS, sudden infant death syndrome.

in this and other studies,[1 2] early term delivery may have detrimental effects on infant morbidity and mortality rates on a population-based level and must be avoided when not medically indicated. When compared with full-term birth, early term birth has also been associated with negative long-term effects, such as increased use of asthma medication, higher prevalence of attention deficit disorders, lower cognition and an over-representation of psychiatric disorders.[12–14] To put the effect size into perspective, our results also show that, compared with being born post-term (a recognised risk group at delivery), being born early term is associated with a 60% higher risk of infant mortality.

Birth weight and infant mortality

A higher infant mortality among SGA infants is well documented at all GAs.[4 15 16] Our results show that very and even moderately SGA infants must be regarded as extra vulnerable to adverse events during the course of their first year of life. In Sweden, SGA is defined as a birth weight of <−2 SD of expected birth weight for GA, a limit approximately corresponding to the 2, 5th percentile. But in international literature, SGA is usually defined as less than the 10th percentile of expected birth weight for GA. In this study, we show that risks of infant, neonatal and postneonatal mortality are increased already at the 10th percentile, which calls for a review of the current Swedish SGA definition. This is the first study on the impact of GA and birth weight for GA on risks of infant, neonatal and postneonatal mortality among term infants that is able to adjust for important socioeconomic, maternal, delivery and infant confounders. After adjusting for these factors, the risk estimates decreased, but associations were still significant. Although adjusted risk estimates may be important from an etiologic perspective, unadjusted risks may be more relevant from a clinical perspective.

Cause of death

Several of the examined causes of death in this study may be preventable in term infants by improved prenatal, delivery and neonatal care routines. First, early term birth per se was associated with increased risks of death by infections and SIDS. We conclude that non-medically indicated deliveries should be avoided at 37–38 gestational weeks when possible. Second, SGA was associated with increased risks of death caused by infections and SIDS, which again puts the focus on intrauterine growth patterns and the importance of appropriate growth surveillance during pregnancy. Third, post-term delivery was associated with increased risks of death by asphyxia, infections and neonatal respiratory disorders. In recent years, induction of delivery has become more common from gestational week 42+0 in Sweden, mainly to avoid intrauterine death. This study suggests that these interventions may be lifesaving also after a live birth. Fourth,

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a high birth weight for GA was associated with an increased risk of death by asphyxia and malignant neoplasms. Among high-risk mothers, that is, mothers with high body mass index and/or diabetes,[17 18] preferable interventions may be normalised prepregnancy body mass index, minimalised weight gain during pregnancy and improved metabolic control. In lack of effective nutritional and metabolic strategies, asphyxia could possibly be avoided by special attention at delivery in this risk group.

CONCLUSIONS

To the field of studies on infant mortality among term infants, our study adds detailed analyses of the relationships between GA and birth weight for GA and risks of neonatal and postneonatal mortality and causes of infant death. Our main conclusions are that non-medically indicated deliveries before 39 weeks gestation should be avoided when possible and that extra caution should be taken in term pregnancies with suspected severe or moderate intrauterine growth restriction. We also conclude that at least some of the infant mortality among non-malformed term infants might be prevented by improvements in antenatal and neonatal care.

Contributors All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis, and the study hypothesis arose before inspection of the data. MA has contributed to the design and conduct of the study; collection, management, analysis and interpretation of the data; and preparation of the manuscript. A-KEB has contributed to the design and conduct of the study, interpretation of the data and review of the manuscript. A-KW has contributed to the design and conduct of the study, interpretation of the data and review of the manuscript. SC has contributed to the design and conduct of the study; collection, management and interpretation of the data; and review of the manuscript. The final version of the manuscript has been approved by all authors.

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Competing interests None.

Ethics approval Ethics approval was provided by the Ethics Committee at Karolinska Institutet, Stockholm.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The statistical code is available from the corresponding author (maria.altman@ki.se). Participants consent was not obtained but the presented data are anonymised and risk of identification is low.

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eTable 1. Distribution of risk factors among survivors and non-survivors at 1 year of age

	Survivors at 1 year of age N=2,142,812		Non-survivors at 1 year of age N=2,687	
	Number	Percent	Number	Percent
Gestational week				
37				
38	98,093	4.6	233	8.7
39	240,909	11.2	368	13.7
40	447,734	20.9	530	19.7
41	594,927	27.8	642	23.9
≥42	450,746	21.0	511	19.0
	310,403	14.5	403	15.0
Birthweight for GA*				
<3				
3-<10	62,433	2.9	202	7.5
10-<25	151,278	7.1	280	10.4
25-75	320,775	15.0	409	15.2
>75-90	1,073,709	50.1	1,234	45.9
>90-97	321,332	15.0	336	12.5
>97	150,037	7.0	146	5.4
	63,248	3.0	80	3.0
Mother's country of birth				
Sweden	1,813,777	84.6	2,248	83.7
Other Nordic	74,833	3.5	132	4.9
Other	244,092	11.4	304	11.3
Missing	10,110	0.5	3	0.1
Education (years)				
≤9	420,545	19.6	720	26.8
10-11	705,962	32.9	923	34.4
12	273,205	12.7	255	9.5
13-14	227,704	10.6	248	9.2
≥15	156,238	7.3	182	6.8
Missing	359,158	16.8	359	13.3
Age at delivery (years)				
<20	50,452	2.4	146	5.4
20-24	1,164,397	54.3	1,544	57.5
25-29	627,463	29.3	688	25.6
30-34	254,265	11.9	246	9.2
≥35	46,235	2.2	63	2.3
Parity				
1	899,586	42.0	1,008	37.5
2	1,105,547	51.6	1,385	51.5
3	122,354	5.7	258	9.6
≥4	15,325	0.7	36	1.3
Smoking habits				
Non-smoker	1,627,384	75.9	1,663	61.9
1-9 cigarettes daily	245,426	11.5	474	17.6
≥10 cigarettes daily	137,825	6.4	373	13.9
Missing	132,177	6.2	177	6.6
Diabetes				
Yes	19,677	0.9	25	0.9
No	2,123,135	99.1	2,662	99.1

	Survivors at 1 year of age N=2,142,812		Non-survivors at 1 year of age N=2,687	
	Number	Percent	Number	Percent
Chronic hypertension				
Yes	9,820	0.5	16	0.6
No	2,132,992	99.5	2,671	99.4
Preeclampsia				
Yes	38,946	1.8	46	1.7
No	2,103,866	98.2	2,641	98.3
PPROM[†]				
Yes	5,086	0.2	16	0.6
No	2,137,726	99.8	2,671	99.4
Birth Year				
1983-1987	424,203	19.8	721	26.8
1988-1992	525,485	24.5	912	33.9
1993-1997	451,479	21.1	460	17.1
1998-2002	388,923	18.2	328	12.2
2003-2006	352,722	16.5	266	9.9
Mode of delivery				
Cesarean section	237,703	11.1	560	20.8
Vaginal instrumental	145,363	6.8	241	9.0
Vaginal non-instrumental	1,759,746	82.1	1,886	70.2
Infant's sex				
Male	1,092,688	51.0	1,537	57.2
Female	1,050,124	49.0	1,150	42.8

*Gestational Age

[†]Preterm Premature Rupture Of the Membranes

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.