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## Adverse Infant Outcomes Associated with Discordant Gestational Age Estimates

Nils-Halvdan Morken<sup>a,b</sup>, Rolv Skjærven<sup>a</sup>, Jennifer L. Richards<sup>c</sup>, Michael R. Kramer<sup>c</sup>, Sven Cnattingius<sup>d</sup>, Stefan Johansson<sup>d,e</sup>, Mika Gissler<sup>f</sup>, Siobhan M. Dolan<sup>g</sup>, Jennifer Zeitlin<sup>h</sup>, Michael S. Kramer<sup>i</sup>, and for the PREBIC Epidemiology Working Group<sup>†</sup>

<sup>a</sup>Departments of Global Public Health and Primary Care, University of Bergen, Bergen, Norway

<sup>b</sup>Clinical Science, University of Bergen, Bergen, Norway <sup>c</sup>Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA <sup>d</sup>Clinical Epidemiology Unit, T2, Department of Medicine Solna, Karolinska University Hospital <sup>e</sup>Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden <sup>f</sup>Information Services Department, National Institute for Health and Welfare, Helsinki, Finland <sup>g</sup>Department of Obstetrics and Gynecology and Women's Health, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY <sup>h</sup>Inserm UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team (Epopé), Center for Epidemiology and Statistics Sorbonne Paris Cité, DHU Risks in pregnancy, Paris Descartes University, Paris, France <sup>i</sup>Departments of Pediatrics and of Epidemiology, Biostatistics and Occupational Health, McGill University Faculty of Medicine, Montreal, QC, Canada

### Abstract

**Background**—Gestational age estimation by last menstrual period (LMP) vs. ultrasound (or best obstetric estimate in the US) may result in discrepant classification of preterm vs. term birth. We investigated whether such discrepancies are associated with adverse infant outcomes.

**Methods**—We studied singleton livebirths in the Medical Birth Registries of Norway, Sweden and Finland and US live birth certificates from 1999 to the most recent year available. Risk ratios (RR) with 95% confidence intervals (CI) by discordant and concordant gestational age estimation for infant, neonatal and post-neonatal mortality, Apgar score <4 and <7 at 5 min, and neonatal intensive care unit (NICU) admission were estimated using generalised linear models, adjusting for maternal age, education, parity, year of birth, and infant sex. Results were presented stratified by country.

**Results**—Compared to infants born at term by both methods, infants born preterm by ultrasound/best obstetric estimate but term by LMP had higher infant mortality risks (range of adjusted RRs 3.9 to 7.2) and modestly higher risks were obtained among infants born preterm by LMP but term

*Correspondence:* Nils-Halvdan Morken, Department of Global Public Health, University of Bergen, Bergen, Norway. nils-halvdan.morken@kk.uib.no.

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### Supporting Information

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by ultrasound/best obstetric estimate (range of adjusted RRs 1.6 to 1.9). Risk estimates for the other outcomes showed the same pattern. These findings were consistent across all four countries.

**Conclusions**—Infants classified as preterm by ultrasound/best estimate, but term by LMP have consistently higher risks of adverse outcomes than those classified as preterm by LMP but term by ultrasound/best estimate. Compared with ultrasound/best estimate, use of LMP overestimates the proportion of births that are preterm.

### Keywords

Gestational age estimation; last menstrual period; ultrasound; best obstetric estimate; infant outcome

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### Background

Preterm birth, defined by the World Health Organization as a delivery before 37 completed gestational weeks, is the most important cause of infant and neonatal morbidity and mortality worldwide.<sup>1</sup> The requirement for defining preterm birth is valid estimation of gestational age. However, this estimation is often an approximation of the elapsed time from conception to delivery. Time from conception is rarely known with certainty, except in pregnancies conceived after assisted reproductive treatment.

Currently, two methods are mainly used to estimate gestational age: (1) the elapsed time from the first day of the last menstrual period (LMP); and (2) an ultrasound estimate based on fetal measurements which are converted into gestational age using established nomograms. Both methods have limitations. Errors in recall, irregular menstrual cycles or post-implantation bleeding can affect the LMP estimate. Ultrasound measurement of the crown-rump length is the most accurate estimate of gestational age in the first trimester, while biparietal diameter provides the most accurate estimate in early second trimester ultrasound.<sup>2</sup> However, fetal sex and early growth restriction affect fetal size, even in early pregnancy.<sup>3</sup> Thus, gestational age estimation by LMP vs. ultrasound (or best obstetric estimate in the US, which takes into account all perinatal factors and assessments including ultrasounds) will affect the estimation of gestational age and classification of preterm birth.<sup>4</sup>

Several authors have reported that discrepancies in LMP vs. ultrasound estimates of gestational age are associated with adverse infant outcome.<sup>5–8</sup> Given the importance of research and public health surveillance on the short- and long-term health consequences of preterm birth,<sup>1</sup> variations in rate of preterm birth caused by differences in method of estimating gestational age are of particular interest.

Comparison of preterm birth data and infant outcomes between countries are challenging due to changes in practice patterns and vital statistics reporting and varying methods of estimating gestational age. However, it is possible that the method of estimation of gestational age may distort cross-country comparison of adverse infant outcomes. By using medical birth registry data from three Nordic countries and US live birth certificate data, we estimated the risks of adverse neonatal outcomes and infant mortality in gestations with discordant gestational age as estimated by LMP and ultrasound or best obstetric estimate.

## Methods

This study is based on all singleton live births registered in the Medical Birth Registries of Norway, Sweden and Finland and US live birth certificates since 1999. The most recent and complete data available from each country were provided: Norway until 2009; Sweden and US until 2012; and Finland until 2014. Pregnancies with gestational ages from 22 weeks +0 days to 41 weeks +6 days were included (based on ultrasound in the Nordic countries and best clinical/obstetric estimate in US vital statistics data). Preterm and term births were defined as a gestational age of 36 completed weeks or less (i.e. 36 weeks +6 days) and 37 weeks or more (i.e. 37 weeks +0 days) respectively. Pregnancies were categorised into concordant gestational estimates (term by both LMP and ultrasound or preterm by both LMP and ultrasound) and discordant gestational estimates (preterm by LMP and term by ultrasound or term by LMP and preterm by ultrasound). In the US, ultrasound dating is not directly available in birth registries, instead births include a 'clinical estimate' (1989 revision of birth certificate) or an 'obstetric estimate' (2003 revision of birth certificate), reflecting information available at birth, including the ultrasound.<sup>9</sup> Births with missing clinical or obstetric estimate, or for which the clinical or obstetric estimate was imputed for missing LMP estimate, were restricted out of the analyses. Pregnancies categorised as term by LMP and ultrasound/obstetric estimate in each country were used as the reference category in all analyses. To minimise misclassification of gestational age, data were cleaned by using the Alexander method to exclude births with incompatible birthweights and gestational age.<sup>10</sup>

We estimated the risks of infant (death <1 year of life), neonatal (death 0–27 days of life), and post-neonatal (death 28 days to <1 year) mortality, low 5-m Apgar score (<4 or <7), and neonatal intensive care unit (NICU) admission. Sweden could not provide data on NICU admission. In the US data, NICU-admission was available only from 2003 to 2012 and only a limited number of states reported this outcome.

Crude and adjusted risk ratios (RRs) with 95% confidence intervals (CIs) were calculated using generalised linear models (STATA version 12.1 [Norway and Sweden] and SAS version 9.4 [Finland and the US]). RRs were adjusted for maternal age in five categories (<20, 20–24, 25–29, 30–34, or 35 years), parity (nulliparous or multiparous), year of birth (continuous variable), and infant sex. For Norway and Sweden, RRs were adjusted for maternal education in three categories (<11, 11–14, or 15 years). In Finland, maternal education during pregnancy was not available; socio-economic status based on maternal occupation during pregnancy was used instead. For the US, maternal education was categorised into <12 years (completed less than high school), 12–15 years (completed high school through some college), and 17 years (completed 4-years college) to align with the education categories in the Nordic countries. However, education was reported differently on US birth certificates between the 1989 and 2003 revisions. The variable from the 1989 version was recorded as 0–17 years of schooling, whereas the 2003 revision uses categories: 8th grade or less, 9th–12th grade (no diploma), high school graduate, some college credit, associate degree, bachelor's degree, master's degree. Comparable analytic categories were created as follows: <12 years included 8th grade or less and 9th–12th grade; 12–15 years included high school graduation, some college credit but not a degree and associate degree; 16 years included bachelor's degree, master's degree and doctorate degree.

Sensitivity analyses were performed for each country by using the z-score method. Infant birthweights were standardised into z-score taking gestational age into account. In a similar way as with the Alexander method, infants with z-scores by birthweight  $<-4$  or  $>4$  were excluded in these analyses. Specific sensitivity analyses were performed in the US data (stratification by version of birth certificate and adjustment for version of birth certificate) to assess impact on differential registration of education and gestational age across study period. Additionally, to assess the impact of clustering (repeated pregnancies to the same mother), a sub-analysis was performed in the Norwegian dataset, using generalised linear models with robust estimation of standard errors (STATA, version 12.1). We also compared births classified as term by LMP but preterm by ultrasound to births classified as preterm by both methods, by restricting both groups to be within 10 days from the cut-off day (259 days of gestation) by ultrasound/best obstetric estimate.

The use of register-based and live birth certificate data is exempt from ethics review in Finland and the US. Aggregated data from Sweden were provided and such data are also exempt from ethics review. In Norway, linked data on maternal level of education were obtained from the national education database. The use of these data was approved by the regional ethics committee, REK VEST, Norway (2009/1868).

## Results

Numbers and characteristics of the datasets by country are presented in Table 1. In all countries, numbers of infants classified as preterm by LMP but term by ultrasound were higher than numbers of infants classified as term by LMP but preterm by ultrasound. The proportion of infants classified as preterm by LMP but term by ultrasound were more than twice the proportion of infants classified as term by LMP but preterm by ultrasound in the United States and Finland, whereas in Sweden and Norway, these groups were almost equal in size. Additionally, the proportion of discordant records was 6% in the United States, while corresponding rates were lower in Finland (2.1%), Sweden (2.5%), and Norway (3.4%).

Compared to infants classified as preterm by LMP and term by ultrasound or clinical estimate, infants classified as term by LMP and preterm by ultrasound (or clinical estimate in the US) had lower mean birth-weight and higher proportion of primiparous mothers in all four countries. Pregnancies with discordant gestational age estimation tended to have lower level of education when compared to pregnancies with concordant gestational age estimation (Table 1, Norway, Sweden, and the United States).

RR's by outcome and method of data cleaning are presented as crude and adjusted estimates in Supporting Information, Tables S1 to S8 (available online) for Norway, Sweden, Finland, and the United States respectively. A summary of adjusted RRs for all four countries is presented in Table 2. Compared to infants classified as term by both methods, risks of all adverse outcomes studied (including infant mortality, neonatal mortality, post neonatal mortality, Apgar  $<4$  at 5 min, Apgar  $<7$  at 5 min, and NICU admissions) were highest for infants classified as preterm by both methods. For infant mortality, the range of adjusted RRs was from 16.9 in the US to 23.1 in Finland. RRs for neonatal mortality ranged from 29.5 in Norway to 40.0 in Finland. Post neonatal mortality showed RRs ranging from 6.1 in

the US to 9.2 in Sweden. RRs for Apgar <4 and Apgar <7 at 5 min ranged from 9.0 in Norway and 7.3 in Sweden to 15.7 and 8.8 in the US respectively. For NICU admissions, RRs ranged from 9.7 in Finland to 13.7 in the US (Sweden did not have data available on NICU admission).

Risks of all adverse outcomes were consistently higher for infants classified as term by LMP but preterm by ultrasound/obstetric estimate than for infants classified as preterm by LMP but term by ultrasound. Compared with infants classified as term by both methods infants classified as preterm by LMP and term by ultrasound also had elevated risks, but to a more modest degree. For example, RRs for infant mortality were 7.1 in Sweden and 7.2 in Finland for infants classified as term by LMP and preterm by ultrasound, but 1.6 and 1.7, respectively, for infants classified as preterm by LMP and term by ultrasound. The same pattern held for neonatal and post-neonatal mortality, Apgar score <4 and <7 at 5 min and NICU admission. Data from the US had more precise estimates (narrower confidence intervals), owing to the very large number of births (>40 million livebirths for most outcomes).

Sensitivity analyses in each country, using the z-score method, yielded similar results for mortality and other outcomes (details are available in the online Tables S2, S4, S6, and S8). In the US data, stratification by and adjustment for version of birth certificate (1989 and 2003 versions) did not change the estimated RR's. The sub-analysis in the Norwegian data, accounting for the effect of repeated pregnancies in the same mother, only minimally affected risks of all outcomes (data not shown).

Risks of adverse outcomes were similar when comparing births classified as term by LMP but preterm by ultrasound to births classified as preterm by both methods and restricting both groups to be within 10 days from the cut-off day (259 days of gestation) by ultrasound/best obstetric estimate.

## Comment

This analysis of data from Norway, Sweden, Finland, and the United States demonstrates that both groups with discordant gestational age estimates had consistently higher risks of adverse perinatal outcomes than those classified as term by both methods. These results show that discrepancy between methods to estimate gestational age may be a predictor for infant mortality and other adverse pregnancy outcomes in all four study countries.

Despite some variability in size of the discordant groups, risk estimates of adverse outcomes were consistent across study countries. The United States had the highest proportion of preterm birth and of small-for-gestational-age births, which could contribute to the higher proportion of infants classified as preterm by LMP but term by ultrasound (4% in the United States vs. 1–2% in the Nordic countries). There was little difference, however, in the proportion of infants classified as term by LMP but preterm by ultrasound across study countries.

One possible explanation for the higher risk in the discordant groups could be poorly recorded LMP. In our analysis, births classified as term by LMP but preterm by ultrasound/

obstetric estimate may reflect random errors in recall of LMP, preference for estimating the LMP as the first day of the month in which it occurred (as opposed to the exact day of the month which is harder to remember), or irregular menses with longer menstrual cycles. Births classified as preterm by LMP but term by ultrasound/obstetric estimate may also reflect random errors in recall of LMP or underestimation of gestational age by women's estimation of their LMP as the last day of the month, or owing to vaginal bleeding early in pregnancy, which can be mistaken for the LMP. Any of these mechanisms may be a marker of other unmeasured confounders such as pregnancy intendedness or lack of preparation for pregnancy, which are associated with increased risk of adverse perinatal outcomes. Other explanations include unreliable ultrasound estimate (such as no performed ultrasound or scans obtained late in pregnancy), infants being truly preterm, or both measures being correct because the infants are growth-restricted.

In all four countries, we found higher risks in infants that were classified as term by LMP but preterm by ultrasound/best obstetric estimate. Higher occurrence of risk factors for discordance, such as low education could be one explanation. We did find lower level of education in pregnancies with discordant gestational age estimation (Table 1). This is in accordance with previous findings that social factors are associated with poor reporting of LMP.<sup>11,12</sup> Other explanations are a higher proportion in this group of true preterm, as ultrasound is a more reliable measure than LMP in most cases<sup>13-15</sup> or that this group of infants represents early growth restriction to a greater extent than the preterm/term group.

It is interesting that births classified as term by LMP but preterm by ultrasound have far lower risks of adverse outcomes than births classified as preterm by both methods. In the sensitivity analyses, risks were similar, when restricting both groups to be within 10 days from the cut-off day (259 days of gestation) by ultrasound/best obstetric estimate, suggesting that these births are more likely to represent late preterm births than those classified as preterm by both methods.

Previous work comparing different methods of gestational age estimation on risks of infant morbidity and mortality have often focused on infants born extremely (<28 weeks) or very preterm (28-31 weeks).<sup>16-18</sup> Until recently, studies have tended to ignore infants born moderately (32-33 weeks) or late preterm (34-36 weeks), as their outcomes were thought to be similar to infants born at 37 weeks and above. Several studies have now shown that late preterm infants do have higher risks of adverse outcomes compared to infants born at term.<sup>19</sup> A large Swedish registry-based study of more than 700 000 singleton pregnancies (live and stillbirths) found that pregnancies with an expected date of delivery postponed by 7-21 days (fetuses were smaller than expected by LMP) had an 87% increased risk of neonatal death (OR 1.87, 95% CI 1.67, 2.09) and an 18% increased risk of an Apgar score <7 at 5 min (OR 1.18, 95% CI 1.11, 1.24).<sup>5</sup> Pregnancies that had their expected date of delivery advanced by 7-21 days (fetuses were larger than expected by LMP) did not have increased risks of these outcomes.<sup>5</sup> The author concluded that the increased risk of neonatal death and low Apgar scores seen in fetuses that were smaller than expected by LMP was a reflection of early growth restriction and disturbances in fetal/placental development.

The increased risk of adverse perinatal outcomes for pregnancies with discordant gestational age estimations based on LMP vs. clinical estimate was confirmed in a US vital statistics study of more than 3 million singleton livebirths.<sup>20</sup> Agreement between the two methods of estimating gestational age was greatest for extremely preterm (20–27 weeks) and term (37–41 weeks) births. Infants born preterm, between 28–36 weeks by LMP-based estimation of gestational age, showed the greatest discordance between the two methods of estimating gestational age. The authors concluded that factors associated with discordant gestational estimates, which are also risk factors for preterm birth, included teenage pregnancy, low educational attainment, late initiation of prenatal care, high birth order, and no ultrasound use during pregnancy.<sup>20</sup> In our data from the US, many pregnancies may not have an ultrasound performed. Clinical estimate in these cases may reflect dating by LMP or a revised LMP based on other available perinatal factors at reporting.

Recently, the importance and magnitude of the method of gestational age estimation was demonstrated in changes in the US national vital statistics reporting. Beginning with data reporting for 2014, the preterm birth rate was calculated based on the best obstetric estimate rather than LMP. Although LMP-based reporting put the US preterm birth rate at 11.4% for 2013, the preterm birth rate based on the obstetric estimate was 9.6% in both 2013 and 2014.<sup>21</sup> Thus, a sudden dramatic drop in the rate of preterm birth was based on changes in reporting methods, rather than scientific or clinical breakthroughs.

### Strengths and limitations

Our study was performed using population-based data from four countries with preterm birth rates ranging from 5 to 6% in Norway,<sup>22</sup> Sweden<sup>23</sup> and Finland<sup>24</sup> and 10 to 11% in the US.<sup>25</sup> To avoid misclassification by gestational age, we cleaned the data using the Alexander method.<sup>10</sup> In a sensitivity analysis using the z-score by birthweight method, similar results were found. Our study also has some limitations. Due to the form of registration, we were not able to account for clustering effects (repeated pregnancies to the same mother) in all data sets. We were able to take this into account in the Norwegian data. However, risk estimates were only minimally affected. Another limitation of our study is that we did not have clinical information on regularity of menstrual cycles or a method to verify patient report of LMP. Information on socioeconomic status differed across countries, but adjusting for education or maternal occupation did not influence risk estimates within any country. Information on maternal smoking was not available in all countries, and information about other life style factors were lacking. Thus, residual confounding may have affected our results. Each country has a different process for checking data entered into the birth registry or birth certificate, and thus validation processes to check or remove values that seem incorrect may also have differed.

### Interpretation and conclusion

In this study from Norway, Sweden, Finland, and the US, infants who were delivered preterm according to ultrasound dating, but term by LMP dating, had increased risks of mortality, low Apgar scores, and NICU admission. These infants may be ‘true preterm,’ with birthweight appropriate for a preterm gestational age, or term infants whose intrauterine growth was restricted. If a first trimester ultrasound is consistent with LMP dating,

pregnancy dating can be established and growth followed. A second-trimester ultrasound that reveals a smaller fetus than expected would suggest early growth restriction. If the LMP is uncertain and/or a late second trimester ultrasound suggests discordance with that LMP, then dating uncertainty is more likely, which will raise concern of pregnancy management. From a public health and vital statistics standpoint, a growing consensus supports use of ultrasound or obstetric estimate for more accurate gestational age assessment. Thus, many countries, including those examined in this study, are moving in that direction.

A valid assessment of gestational age is essential in clinical management, clinical trials, epidemiologic studies, and vital statistics. Our multicountry study highlights that discrepant estimates in gestational age assessment are associated with adverse infant outcomes across all four study countries. It seems reasonable to conclude that using the ultrasound/best obstetric estimate to define preterm will yield infants with higher risks of poor outcomes (whether or not they are truly preterm).

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1**

Characteristics of data from Norway (1999–2009), Sweden (1999–2012), Finland (1999–2014), and United States (1999–2012) by concordant and discordant gestational age estimation, using last menstrual period (LMP) and ultrasound (US<sup>a</sup>)

	Term (LMP) Term (US)	Preterm (LMP) Term (US)	Term (LMP) Preterm (US)	Preterm (LMP) Preterm (US)
Norway <i>n</i> = 373 131 (%)	340 470 (91.2)	6 368 (1.7)	6 251 (1.7)	20 042 (5.5)
Maternal age, mean (sd) <sup>b</sup>	29.6 (5.0)	29.6 (5.5)	28.8 (5.3)	29.8 (5.4)
Primiparous (%)	37.5	39.1	45.5	48.1
Maternal education (%)				
<11 years	17.0	24.7	23.9	20.2
11–14 years	34.9	35.9	36.9	36.9
14 years	48.1	39.4	39.2	42.9
Male (%)	49.1	59.7	45.3	55.1
Birthweight, mean (sd)	3553 (473)	3277 (491)	2894 (523)	2309 (729)
Sweden <i>n</i> = 1 009 278 (%)	947 233 (93.8)	12 958 (1.3)	11 942 (1.2)	37 145 (3.7)
Maternal age, mean (sd)	30.1 (5.1)	30.2 (5.6)	29.1 (5.2)	30.2 (5.4)
Primiparous (%)	43.2	44.2	53.3	55.6
Maternal education (%)				
<11 years	23.1	33.3	27.5	26.1
11–14 years	41.2	38.6	43.2	41.3
14 years	35.6	28.1	29.2	32.6
Male (%)	50.6	58.4	47.5	56.3
Birthweight, mean (sd)	3585 (480)	3219 (473)	2856 (486)	2357 (698)
Finland <i>n</i> = 787 405 (%)	739 354 (93.9)	11 903 (1.5)	4 441 (0.6)	31 707 (4.0)
Maternal age, mean (sd)	30.1 (5.3)	30.0 (6.2)	28.9 (5.5)	30.6 (6.2)
Primiparous (%)	40.2	42.3	51.2	49.9
SES <sup>c</sup> (%)				
Lower white collar worker	17.2	13.5	13.9	16.0
Upper white collar worker	34.7	28.8	33.9	34.5
Blue collar worker	13.7	15.8	15.0	14.5
Other or unknown	34.4	41.8	37.2	35.1
Male (%)	51.0	53.6	52.4	56.2
Birthweight, mean (sd)	3575 (467)	3356 (507)	2832 (548)	2393 (732)
USA <i>n</i> = 47 602 926 (%)	41 747 473 (87.7)	2 005 669 (4.2)	864 007 (1.8)	2 985 777 (6.3)
Maternal age, mean (sd)	27.4 (6.1)	26.6 (6.5)	26.7 (6.3)	27.4 (6.5)
Primiparous (%)	40.9	36.2	40.1	43.5
Maternal education (%)				
<12 years	19.2	28.5	24.9	22.1
12–15 years	53.0	54.6	56.2	55.6
16 years	27.8	16.9	18.9	22.4
Male (%)	50.9	53.2	51.7	54.2

	<b>Term (LMP) Term (US)</b>	<b>Preterm (LMP) Term (US)</b>	<b>Term (LMP) Preterm (US)</b>	<b>Preterm (LMP) Preterm (US)</b>
Birthweight, mean (sd)	3404 (458)	3187 (478)	2756 (531)	2310 (736)

<sup>a</sup>In the United States best clinical (1999–2002) and obstetric (2003–12) estimates were used.

<sup>b</sup>Standard deviation

<sup>c</sup>Socio-economic status.

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Risk Ratios (RR's) for adverse neonatal and infant outcomes by method of gestational age estimation and country, using the Alexander method for data cleaning

Table 2

	Last menstrual period	Ultrasound <sup>d</sup>	Norway (n = 373 131) <sup>d</sup>		Sweden (n = 1 009 278)		Finland (n = 787 405) <sup>b</sup>		United States (n = 47 602 926) <sup>c</sup>	
			Adjusted <sup>e</sup> RR 95% CI	Term	Adjusted <sup>e</sup> RR 95% CI	Term	Adjusted <sup>e</sup> RR 95% CI	Term	Adjusted <sup>e</sup> RR 95% CI	Term
Infant mortality <sup>f</sup>	Term	Term	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Preterm	Term	1.9 (1.2, 3.0)	1.6 (1.03, 2.4)	1.6 (1.03, 2.4)	1.7 (1.1, 2.5)	1.6 (1.6, 1.6)	1.6 (1.6, 1.6)	1.6 (1.6, 1.6)	1.6 (1.6, 1.6)
	Term	Preterm	4.0 (2.9, 5.6)	7.1 (5.7, 8.8)	7.1 (5.7, 8.8)	7.2 (5.1, 10.1)	3.9 (3.8, 4.0)	3.9 (3.8, 4.0)	3.9 (3.8, 4.0)	3.9 (3.8, 4.0)
	Preterm	Preterm	19.0 (16.8, 21.4)	21.1 (19.2, 23.1)	21.1 (19.2, 23.1)	23.1 (21.0, 25.5)	16.9 (16.7, 17.1)	16.9 (16.7, 17.1)	16.9 (16.7, 17.1)	16.9 (16.7, 17.1)
Neonatal mortality <sup>g</sup>	Term	Term	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Preterm	Term	2.2 (1.2, 4.0)	1.5 (0.8, 2.7)	1.5 (0.8, 2.7)	2.0 (1.2, 3.5)	1.7 (1.7, 1.8)	1.7 (1.7, 1.8)	1.7 (1.7, 1.8)	1.7 (1.7, 1.8)
	Term	Preterm	4.5 (2.9, 6.9)	10.4 (8.0, 13.5)	10.4 (8.0, 13.5)	9.7 (6.3, 15.0)	5.9 (5.7, 6.1)	5.9 (5.7, 6.1)	5.9 (5.7, 6.1)	5.9 (5.7, 6.1)
	Preterm	Preterm	29.5 (25.3, 34.5)	34.3 (30.4, 38.6)	34.3 (30.4, 38.6)	40.0 (35.2, 45.3)	37.9 (37.4, 38.4)	37.9 (37.4, 38.4)	37.9 (37.4, 38.4)	37.9 (37.4, 38.4)
Post neonatal mortality <sup>h</sup>	Term	Term	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Preterm	Term	1.5 (0.7, 3.2)	1.6 (0.95, 2.8)	1.6 (0.95, 2.8)	1.4 (0.7, 2.5)	1.5 (1.4, 1.5)	1.5 (1.4, 1.5)	1.5 (1.4, 1.5)	1.5 (1.4, 1.5)
	Term	Preterm	3.5 (2.1, 5.8)	4.2 (2.9, 6.1)	4.2 (2.9, 6.1)	4.9 (2.8, 8.5)	2.8 (2.7, 2.9)	2.8 (2.7, 2.9)	2.8 (2.7, 2.9)	2.8 (2.7, 2.9)
	Preterm	Preterm	7.6 (6.0, 9.5)	9.2 (7.8, 10.9)	9.2 (7.8, 10.9)	7.8 (6.5, 9.5)	6.1 (6.0, 6.1)	6.1 (6.0, 6.1)	6.1 (6.0, 6.1)	6.1 (6.0, 6.1)
Apgar <4 at 5 min	Term	Term	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Preterm	Term	1.2 (0.7, 2.1)	1.0 (0.6, 1.5)	1.0 (0.6, 1.5)	1.7 (1.2, 2.4)	1.3 (1.3, 1.4)	1.3 (1.3, 1.4)	1.3 (1.3, 1.4)	1.3 (1.3, 1.4)
	Term	Preterm	2.3 (1.5, 3.5)	3.2 (2.4, 4.2)	3.2 (2.4, 4.2)	4.3 (2.9, 6.3)	3.4 (3.3, 3.5)	3.4 (3.3, 3.5)	3.4 (3.3, 3.5)	3.4 (3.3, 3.5)
	Preterm	Preterm	9.0 (7.8, 10.3)	9.6 (8.6, 10.6)	9.6 (8.6, 10.6)	13.8 (12.4, 15.3)	15.7 (15.5, 15.9)	15.7 (15.5, 15.9)	15.7 (15.5, 15.9)	15.7 (15.5, 15.9)
Apgar <7 at 5 min	Term	Term	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Preterm	Term	1.3 (1.03, 1.7)	1.0 (0.9, 1.2)	1.0 (0.9, 1.2)	1.4 (1.2, 1.6)	1.2 (1.2, 1.3)	1.2 (1.2, 1.3)	1.2 (1.2, 1.3)	1.2 (1.2, 1.3)
	Term	Preterm	2.6 (2.1, 3.1)	2.8 (2.5, 3.2)	2.8 (2.5, 3.2)	3.2 (2.6, 3.8)	3.0 (3.0, 3.1)	3.0 (3.0, 3.1)	3.0 (3.0, 3.1)	3.0 (3.0, 3.1)
	Preterm	Preterm	7.5 (7.0, 8.0)	7.3 (6.9, 7.6)	7.3 (6.9, 7.6)	8.7 (8.3, 9.1)	8.8 (8.8, 8.9)	8.8 (8.8, 8.9)	8.8 (8.8, 8.9)	8.8 (8.8, 8.9)
NICU-admission	Term	Term	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Preterm	Term	2.0 (1.9, 2.2)	Not available	Not available	1.7 (1.6, 1.8)	1.6 (1.5, 1.6)	1.6 (1.5, 1.6)	1.6 (1.5, 1.6)	1.6 (1.5, 1.6)
	Term	Preterm	5.4 (5.2, 5.6)	7.7 (7.3, 8.2)	7.7 (7.3, 8.2)	9.7 (9.2, 10.2)	6.8 (6.9, 6.9)	6.8 (6.9, 6.9)	6.8 (6.9, 6.9)	6.8 (6.9, 6.9)
	Preterm	Preterm	11.3 (11.1, 11.5)	13.7 (13.7, 13.8)	13.7 (13.7, 13.8)	13.7 (13.7, 13.8)	13.7 (13.7, 13.8)	13.7 (13.7, 13.8)	13.7 (13.7, 13.8)	13.7 (13.7, 13.8)

<sup>a</sup>NICU-admission: 345 685 liveborn were included.

<sup>b</sup>Apgar score <4 and <7 at 5 min registered during 2004–14 only: 545 023 liveborn were included.

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<sup>c</sup> Apgar score <4 and <7 at 5 min: 45 491 826 liveborn had complete data, NICU-admission: Only births reported on 2003 revision of US live birth certificate, no national data available as only a limited number of states report this outcome: 17 305 119 included livebirths.

<sup>d</sup> In the United States, clinical estimate of gestation was used for births reported on 1989 revision of US live birth certificate and obstetric estimate of gestation was used for births reported on 2003 revision of US live birth certificate.

<sup>e</sup> RR's were obtained by generalised linear models adjusting for maternal age, level of education, parity, fetal sex, and year of birth.

<sup>f</sup> Death <1 year of life,

<sup>g</sup> Death 0–27 days of life,

<sup>h</sup> Death 28 days to 12 months of age.