Apgar score and the risk of cause specific infant mortality: a population based cohort study of 1,029,207 livebirths

Stamatina Iliodromiti
School of Medicine, University of Glasgow, Glasgow Royal Infirmary, Glasgow G31 2ER, United Kingdom
Stamatina.Iliodromiti@glasgow.ac.uk

Daniel F Mackay
Institute of Health and Wellbeing, University of Glasgow, 1 Lilybank Gardens, Glasgow G12 8RZ, United Kingdom
daniel.mackay@glasgow.ac.uk

Gordon CS Smith
Department of Obstetrics and Gynaecology, University of Cambridge, Rosie Hospital, Cambridge, NIHR Cambridge Biomedical Research Centre, CB2 0SW, United Kingdom
gcss2@cam.ac.uk

Jill P Pell
Institute of Health and Wellbeing, University of Glasgow, 1 Lilybank Gardens, Glasgow G12 8RZ, United Kingdom
jill.pell@glasgow.ac.uk

Scott M Nelson
School of Medicine, University of Glasgow, Glasgow Royal Infirmary, Glasgow G31 2ER, United Kingdom
scott.nelson@glasgow.ac.uk

Address for correspondence:
Professor Scott M Nelson
School of Medicine
University of Glasgow
Room 2.52 Level 2
New Lister Building
Glasgow Royal Infirmary
GLASGOW G31 2ER

Tel: 00 44 141 201 8581
Tel: 00 44 141 201 8615
Email: Scott.Nelson@glasgow.ac.uk

Abstract

Background: The Apgar score has been used globally as an index of early neonatal condition for over 60 years. Given advances in healthcare service provision, neonatal resuscitation and infant care, its current relevance is unclear. The aim of the study was to determine the strength of the relationship between Apgar score at 5 minutes and the risk of neonatal and infant mortality, sub-divided by specific causes.

Methods: Routine discharge and mortality data were linked for all births in Scotland between 1992 and 2010. The relative risks (RR) of neonatal and infant death of neonates with low (0-3) and intermediate (4-6) Apgar scores at 5 minutes referent to neonates with normal Apgar score (7-10) were calculated by binomial log-linear modelling with adjustment for confounders. Analyses were stratified by gestational age at birth, as it was a significant effect modifier. Missing covariate data were imputed.

Findings:

Complete data were available on 1,029,207 eligible livebirths. Across all gestational strata, low Apgar score at 5 minutes was associated with an increased risk of neonatal and infant death (deaths due to anomalies were excluded). However, the strength of the association (adjusted relative risk, 95% CI; referent to Apgar7-10) was strongest at term (P<0.001). A very low Apgar (0-3) was associated with a 359.4-fold risk (95% CI 277.3, 465.9) of early neonatal death, a 30.47 (95% CI 17.99, 51.62) -fold risk of late neonatal death and a 50.23 (95% CI 42.77, 58.98) -fold risk of infant death. Similar associations of a lower magnitude were observed for an intermediate Apgar (4-6). The strongest associations were for deaths attributed to anoxia. There was no association between Apgar score at 5 minutes and the risk of sudden infant death syndrome at any gestational age.

Interpretation: Low Apgar score at 5 minutes was strongly associated with the risk of neonatal and infant death. Our findings support its continued utility in contemporary practice.

Funding: None

Keywords: Apgar score; neonatal mortality; infant mortality; SIDS; anoxia

Introduction

The Apgar score has been used globally as an index of health in the immediate neonatal period for over 60 years [1]. Its ability to assess the need for, and response to, resuscitation has led to it being incorporated into national guidelines and World Health Organisation Policy[2, 3]. By virtue of its associations with short and long term mortality, it is also used as an early surrogate outcome for strategies designed to achieve the Millennium Development Goal of reducing child mortality[4].

Evaluation of the Apgar score at 5 minutes in contemporary populations, where neonatal intensive care provision is routinely available, has been limited[5, 6,7]. A population study of 235,165 births from 1983-1987 suggested an association between low Apgar score at 5 minutes and neonatal mortality[7]. Similar associations were reported in a single centre study of 151,891 singletons from 1988-1998[5]. A more recent population study utilising US birth registry data from 1995-2004, also reported increased crude mortality rates among term and pre-term infants with low Apgar scores at 5 minutes[6]. Importantly, however, none of these studies adjusted for known risk factors for mortality including birthweight, social class, smoking status or previous neonatal death. Furthermore, there was no information on whether the deaths were potentially preventable.

In this study we analysed nationally collected data from Scotland where advanced neonatal resuscitation resources are routinely available to characterise the neonatal, infant and cause specific mortality risk of newborns in relation to their Apgar score 5 minutes. We determined whether these associations persisted after adjustment for risk factors known to increase mortality rates among term and preterm infants, and following exclusion of deaths due to congenital anomalies.

Methods

Study Population

We linked four Scotland-wide databases; the Scottish Morbidity Record 02 (SMR02); the National Records for Scotland (NRS); the Scottish Stillbirth and Infant Death Survey (SSBIDS); and the General Registrar for Scotland's death certificate database. The SMR02 collects information on all women discharged from Scottish maternity hospitals, including maternal and infant characteristics, clinical management and obstetric complications (full lists of data collected are available here: http://www.adls.ac.uk/nhs-scotland/maternity-inpatient-and-day-case-smr02/?detail). The SMR02 is subjected to regular quality assurance exercises. The most recent compared a 4.4% sample of SMR02 returns (n=2,531) to case records and demonstrated that all of the data items used in our study were over 90% complete and accurate[8]. Gestational age has been confirmed by ultrasound in the first half of pregnancy in more than 95% of women in the United Kingdom since the early 1990's. The NRS (http://www.nrscotland.gov.uk) registers all stillbirths and infant deaths and the SSBIDS (http://www.isdscotland.org/Health-Topics/Maternity-and-Births/Stillbirth-and-Infant-Deaths/SPIMMR-Background-Information.pdf) then collects additional information from the SSBIDS coordinator at the relevant hospital; who is either an obstetrician, paediatrician or midwife. The coordinator submits copies of the relevant case summaries, post-mortem reports, discharge letters and perinatal mortality meeting reports as well as completing a questionnaire. The General Registrar for Scotland collates information from death certificates including the primary and secondary causes of death (http://www.gro-scotland.gov.uk). The advisory committee of the Information Services Division (ISD) of the National Services Scotland awarded approval for records' access and linkage.

Inclusion criteria and definitions

We obtained SMR02 data on all infants delivered in Scotland between 1st January 1992 and 31st December 2010 inclusive, the latter equating to the most recent data available at the time of data extraction. Our analyses were restricted to singleton births, in women aged over 10 years, with a gestational age at delivery between 24 and 44 weeks inclusive. We excluded infant deaths due to congenital anomalies or isoimmunisation. Death ascribed to congenital anomaly was defined as any structural or genetic defect incompatible with life or potentially treatable but causing death.

Postcode of residence is recorded on the SMR02 record and is used to allocate individuals to an area-based socioeconomic decile of the general population using the 2004 Scottish Index of Multiple Deprivation (SIMD) (http://www.scotland.gov.uk/Publications/2005/01/20458/49127). The index is derived from 31 area markers of deprivation measures across the domains of health, education, housing, current income, employment access and crime, that are applied to each postcode data zones. There are 6,505 data zones across Scotland with a mean population of 750.

Apgar score at 5 minutes of age was categorised into three ordinal groups; low (Apgar 0-3), intermediate (Apgar 4-6) and normal (Apgar 7-10)[2]. The primary outcomes studied were: early neonatal (from birth to up to seven days of life) deaths, late neonatal (from day seven up to day 28), and overall neonatal (up to four weeks) and overall infant deaths (up to one year). The secondary outcome was cause specific mortality. Sudden infant death syndrome (SIDS) was defined as infant deaths for which the primary cause was recorded as an International Classification of Diseases 10 (ICD 10) code of R95 or an ICD 9 code of 798.0[9]. Neonatal

causes were coded using a modification of the Wigglesworth paediatric classification, including anoxia and infection[10]. The definition of anoxia was broad and included hypoxia, acidosis, and asphyxia. In preterm neonates, hyaline membrane disease was included as an additional cause of death, in contrast lung immaturity is restricted by definition to neonates born under 27 weeks gestation and was not considered as a secondary outcome.

Confounders and risk factors

We adjusted the risk of death for maternal age, parity, socioeconomic deprivation, year of delivery, marital status, smoking status, history of neonatal death, mode of delivery (vaginal, abdominal) and timing of delivery (elective included all induced labours and programmed caesarean sections, unplanned included all the spontaneous onset labours and emergency caesarean sections), sex of the baby and birthweight (categorised according to sex, gestation –specific centiles : 1^{st}-10^{th} centile, 11^{th}-90^{th} centile and > 90^{th} centile). The 11^{th}-90^{th} centile category was treated as the referent category for the regression models and the 1-10^{th} centile referred to the small for gestation category. Gestation of delivery was examined in stratified analyses in accordance with recent recommendations; 24-31^{+6}, 32-33^{+6}, 34-36^{+6}, 37-38^{+6}, 39-40^{+6}, 41-41^{+6}, $\geq$ 42 weeks[11].

Statistical Analyses

Median and interquartile ranges were used for continuous variables and Kruskal Wallis test for descriptive statistics. Chi-square tests were used for comparison of categorical variables between groups. Relative risks (RR) of the outcomes were modelled with a binomial log-linear regression model before and after adjustment for confounders. Missing values for confounders were imputed (n=5) and the regression models were performed with imputed values replacing missing values. The significance of interaction terms was assessed using the

likelihood ratio test. The level of $p<0.05$ was considered as statistically significant. Sensitivity analysis was performed to examine whether the associations between Apgar scores and mortality in the dataset with the complete set of covariates differed from those in the imputed dataset. In addition, sensitivity analysis was performed to test whether the associations differed across epochs of year of delivery (four epochs: 1992-1996, 1997-2000, 2001-2005 and 2006-2010). All analyses were performed with Stata (version 12, StataCorp LP, College Station, TX).

Results

Between 1st January 1992 and 31st December 2010, there were 1,062,390 deliveries in Scotland. We excluded 15,426 (1.5%) non-singleton deliveries, 1,367 (0.13%) with a gestational age outside the range 24 to 44 weeks gestation, 5,158 (0.49%) stillbirths, 1,999 (0.19%) infant deaths due to congenital anomalies or rhesus isoimmunisation, and 9,792 (0.92%) where the Apgar score at 5 minutes of age was not recorded. Some records had multiple exclusions. Therefore, the study group comprised the remaining 1,029,207 deliveries.

Among these deliveries, there were 1,395 (0.14%) neonatal deaths, of which 967 (0.09%) were early neonatal deaths and 428 (0.04%) were late neonatal deaths. Overall, there were 2,307 (0.22%) infant deaths. 1,050 (45.5%) were born at term (37 weeks and over), of which 388 (37%) were due to SIDS, 245 (23.3%) were due to anoxia, and 57 (5.43%) were due to infection. 1,257 infant deaths (54.5% of total infant deaths) were born preterm, with 275 (21.9%) attributed to lung immaturity, 201 (16%) attributed to hyaline membrane disease, 190 (15.1%) attributed to infection, 120 (9.5%) attributed to anoxia and 80 (6.4%) attributed

to SIDS. Figure 1 demonstrates a flowchart of the selected cohorts including the denominators for each analysis.

Table 1 shows the maternal characteristics, delivery details and frequency of the primary outcomes relative to the Apgar grouping at 5 minutes. The majority of neonates (98.46%) had a normal Apgar score at 5 minutes. Women who delivered infants with a low Apgar (0-3) at 5 minutes were more likely to be young, smokers, multiparous and have an obstetric history of neonatal death compared with women who delivered neonates with a normal Apgar at 5 minutes. A low Apgar score at 5 minutes was more frequent among infants delivered preterm or by caesarean section.

The crude rate of neonatal and infant mortality declined markedly and progressively with advancing gestational age (Supplementary Table 1) and with increased Apgar score at 5 minutes. However, there was a significant interaction between gestational age ($p<0.001$) and Apgar score category at 5 minutes, hence, subsequent analyses were stratified by gestational age. On the contrary, the interaction of Apgar score category at 5 minutes with birth-weight centile was not significant ($p=0.36$), nor the interaction of Apgar score at 5 minutes with epochs of year of delivery ($p=0.26$). The relative risk of infant death associated with low Apgar score at 5 minutes became progressively greater with advancing gestational age (Figure 2, Supplementary Table 2). The relative risk of neonatal and infant mortality associated with a low Apgar score at 5 minutes peaked at 41 to 41^{+6} weeks, and subsequently declined, although remaining highly statistically significant. The patterns of absolute and relative risks of death were not materially altered when the analysis was restricted to complete cases (Supplementary Table 3). Supplementary Table 4 presents the adjusted

relative risk for neonatal and infant mortality of other risk factors complimentary to low and intermediate Apgar scores.

Table 2 and Supplemental Figure 1show the absolute infant mortality rates and the cause specific mortality rates for term and preterm infants stratified by Apgar scoring at 5 minutes. Among term infants, the association between low Apgar and the risk of death was strongest for deaths due to anoxia (relative risk 961.7, 95% CI 681.3, 1357.5). However, low Apgar at 5 minutes was also associated with death attributed to infection (relative risk 49.3, 95% CI 24.1, 100.9), although the association was clearly weaker than that for anoxia. Among preterm infants, there was a similar pattern of stronger associations with death attributed to anoxia (relative risk 141.7, 95% CI 90.1, 222.8) than with infection (relative risk 13.0, 95% CI 9.1, 18.7). Additionally, there was an association between low Apgar at 5 minutes and the risk of death attributed to hyaline membrane disease. In both term (p=0.68) and preterm (p=0.97) infants mortality attributable to SIDS was unrelated to the Apgar score at 5 minutes. Preterm infants were more than three times likely to die from SIDS than term neonates independent of Apgar score at 5 minutes (i.e. 14 infant deaths per 10,000 live-born among preterm neonates with normal Apgar score at 5 minutes as compared to 4 infant deaths per 10,000 live-born among term neonates with normal Apgar score).

Discussion

The Apgar score was first described more than 60 years ago[1, 12]. Despite huge changes in paediatric care and massive falls in the risk of infant death in the intervening period, we found that the Apgar score at 5 minutes was still extremely strongly associated with the risk of neonatal and infant death in Scotland between 1992 and 2010. The associations with neonatal and infant mortality were present at both term and preterm gestations and robust to

adjustment for a wide range of confounders[13]. We demonstrate that a low Apgar score at 5 minutes was more strongly associated with neonatal and infant mortality attributable to anoxia or infection with an additional association with hyaline membrane disease in preterm infants. The associations were, however, cause specific. For example, there was no significant association between Apgar score at 5 minutes and the risk of SIDS, the leading single cause of post neonatal infant death.

There is increasing recognition that there is substantial variability in outcomes among neonates delivered at 37 and beyond completed weeks, despite all being classed as "term"[14]. We therefore examined gestation cut points for stratification in accordance with recent recommendations[11]. Previous studies stratified the risk of neonatal mortality in relation to low Apgar score at 5 minutes by birthweight rather than by gestation, despite birthweight being a function of gestational age and intrauterine growth[7, 15, 16]. Our analysis demonstrated that gestational age rather than birthweight is an effect modifier of this relationship. In premature infants, a low Apgar score may reflect intrinsic physiological immaturity and inadequate capacity for response rather than abnormal autonomic, cardiovascular and respiratory function in term infants[17, 18].

Gestational age at birth has consistently been shown to exhibit an inverse association with neonatal and infant mortality[19]. The net effect of a low Apgar score at 5 minutes on the relative risk of both neonatal and infant mortality is thereby smaller for premature infants than observed at term. Although the Apgar score is associated with mortality at all gestations[5-7, 20], the magnitude of the effect changes across the distribution of gestational ages because the background mortality risk of each gestational group varies. Hence, a normal

score in preterm infants, unlike full term infants, does not necessarily predict a good outcome[13].

To our knowledge, this is the first study linking the effect of a low Apgar score at 5 minutes with specific causes of infant mortality. At both term and preterm gestations, infants with a low Apgar score at 5 minutes were more likely to die from a cause attributable to anoxia rather than other causes. Fetal hypoxia and acidosis, as detected by cord blood gas, are frequently associated with a reduction in the Apgar score[5, 21]. Similarly, maternal and fetal infections have been associated with lower Apgar scores[22, 23]. Although a nested case control study of 148 cases reported an inverse trend with Apgar at 5 minutes score and risk of SIDS[24], we did not observe this. This may reflect our greater sample size, as our findings are consistent with two larger case control studies[25, 26].

Our study included more than one million deliveries. We included all eligible deliveries in Scotland over a nineteen year period, thereby avoiding selection bias and facilitating extrapolation to other populations with similar baseline and ethnic characteristics. We linked four national datasets to maximise data completeness. The routine data sources are subject to quality assurance checks and have been shown to perform well in terms of completeness and accuracy. The detail provided by these datasets allowed us to examine a range of different outcomes and adjust for an extensive series of potential confounders and consider effect modifiers. We used robust methodology to calculate the relative risk of the outcome for low and intermediate Apgar scores at 5 minutes compared with neonates with a normal Apgar score with and without adjustment for covariates[20]. We acknowledge that our analyses had some limitations; Apgar score at 5 minutes is not subject to quality control measures but reflects routine clinical practice [27]. The individual components of the Apgar score at 5

minutes were not available to examine which was the strongest predictor of mortality, but our findings add weight to the continuation of the Apgar score at 5 minutes in its current form. We did not have data on the Apgar score at 1 minute, but there is evidence that the Apgar score at 5 minutes has greater predictive performance [15]. We assumed that the population remained relatively stable without infants selectively leaving Scotland and thereby introducing systematic error and that the complete dataset for the multivariable models were reflective of the population. That the effect size in the imputed models is not substantially attenuated in comparison to complete cases supports this assumption.

The Apgar score was developed to provide an early assessment of neonatal condition and stratify care when healthcare resources and effective interventions were limited. Our study demonstrates that sixty years after its introduction it continues to be prognostic for neonatal and infant mortality in contemporary developed populations.

Contributors

SI searched the scientific literature, did the statistical analysis and participated in data interpretation and drafted the manuscript. DFM contributed to the statistical analysis and data interpretation JPP obtained the data and contributed to data interpretation. GCSS contributed to data interpretation. SMN conceived the study, contributed to the statistical analysis, data interpretation and drafted the manuscript. All authors contributed to preparation of the report and approved the final version.

Declaration of interests

All authors declare that they have no competing interests

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None

Panel: Research in context

Systematic Review

PubMed and MEDLINE were searched for reports published until February 2014. Search terms for Apgar score (keyword: Apgar*) and infant mortality (keywords: neonatal death, neonatal mortality, infant death, infant mortality, neonate and infant) were combined. The reference lists of the selected papers were hand-searched for other potentially relevant papers. We have cited all the relevant reports in the main text but we were primarily interested in studies relevant to our research question and referring to contemporary populations[1-3].

Interpretation

The Apgar score at 5 minutes of life, is an aggregate score of five readily identifiable neonatal characteristics; skin colour, heart rate, respiratory effort, muscle tone and reflexes. Each category is assigned a score of 0, 1 or 2 depending on the observed condition. Despite recent advances in neonatal intensive care and routine provision of neonatal resuscitation we confirm that 60 years after its introduction the Apgar score at 5 minutes is still predictive of neonatal and infant mortality. In accordance with national guidelines we categorised Apgar score in three categories (low, intermediate and normal) [4]. We confirm that infants with low and intermediate Apgar score have a substantially increased risk of death within the first year of life and for the first time demonstrate that these associations are independent of other confounders/risk factors and particularly marked for term infants. Our novel cause specific analyses demonstrate that the strongest associations were observed for deaths attributed to anoxia. Our study supports the ongoing clinical utility of Apgar scores in contemporary populations.

1. Casey BM, McIntire DD, Leveno KJ. The continuing value of the Apgar score for the assessment of newborn infants. *N Engl J Med* 2001; **344(**7): 467-71.

2. Moster D, Lie RT, Irgens LM, Bjerkedal T, Markestad T. The association of Apgar score with subsequent death and cerebral palsy: A population-based study in term infants. *J Pediatr* 2001; **138**(6): 798-803.

3. Li F, Wu T, Lei X, Zhang H, Mao M, Zhang J. The apgar score and infant mortality. *PLoS One* 2013; **8**(7): e69072.

4. American Academy of Pediatrics. The Apgar score. *Pediatrics* 2006; **117**(4): 1444-7.

References

1. Apgar V. A proposal for a new method of evaluation of the newborn infant. *Current researches in anesthesia & analgesia* 1953; **32**(4): 260-7.

2. American Academy of Pediatrics. The Apgar score. *Pediatrics* 2006; **117**(4): 1444-7.

3. World Health Organisation. Countdown to 2015 for maternal, newborn and child survival: accountability for maternal, newborn and child survival. Geneva, 2013.

4. Lozano R, Wang H, Foreman KJ, et al. Progress towards Millennium Development Goals 4 and 5 on maternal and child mortality: an updated systematic analysis. *Lancet* 2011; **378**(9797): 1139-65.

5. Casey BM, McIntire DD, Leveno KJ. The continuing value of the Apgar score for the assessment of newborn infants. *N Engl J Med* 2001; **344**(7): 467-71.

6. Li F, Wu T, Lei X, Zhang H, Mao M, Zhang J. The apgar score and infant mortality. *PLoS One* 2013; **8**(7): e69072.

7. Moster D, Lie RT, Irgens LM, Bjerkedal T, Markestad T. The association of Apgar score with subsequent death and cerebral palsy: A population-based study in term infants. *J Pediatr* 2001; **138**(6): 798-803.

8. Information Services Division. Data quality assurance. Assessment of maternity data (SMR02) 2008-2009. : NHS Scotland, 2010.

9. Brooke H, Gibson A, Tappin D, Brown H. Case-control study of sudden infant death syndrome in Scotland, 1992-5. *BMJ* 1997; **314**(7093): 1516-20.

10. Information and Statistics Division NHS Scotland. Scottish Perinatal and Infant Mortality and Morbidity report. Edinburgh, Scotland ISD Publications, Common Services Agency, 2008.

11. Spong CY. Defining "term" pregnancy: recommendations from the Defining "Term" Pregnancy Workgroup. *JAMA* 2013; **309**(23): 2445-6.

12. Apgar V, James LS. Further observations on the newborn scoring system. *Am J Dis Child* 1962; **104**: 419-28.

13. Weinberger B, Anwar M, Hegyi T, Hiatt M, Koons A, Paneth N. Antecedents and neonatal consequences of low Apgar scores in preterm newborns: a population study. *Arch Pediatr Adolesc Med* 2000; **154**(3): 294-300.

14. Tita AT, Landon MB, Spong CY, et al. Timing of elective repeat cesarean delivery at term and neonatal outcomes. *N Engl J Med* 2009; **360**(2): 111-20.

15. Drage JS, Kennedy C, Schwarz BK. The apgar score as an index of neonatal mortality. a report from the collaborative study of cerebral palsy. *Obstet Gynecol* 1964; **24**: 222-30.

16. Nelson KB, Ellenberg JH. Apgar scores as predictors of chronic neurologic disability. *Pediatrics* 1981; **68**(1): 36-44.

17. Catlin EA, Carpenter MW, Brann BSt, et al. The Apgar score revisited: influence of gestational age. *J Pediatr* 1986; **109**(5): 865-8.

18. Hegyi T, Carbone T, Anwar M, et al. The apgar score and its components in the preterm infant. *Pediatrics* 1998; **101**(1 Pt 1): 77-81.

19. Liu L, Johnson HL, Cousens S, et al. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet* 2012; **379**(9832): 2151-61.

20. Thorngren-Jerneck K, Herbst A. Low 5-minute Apgar score: a population-based register study of 1 million term births. *Obstet Gynecol* 2001; **98**(1): 65-70.

21. Sykes GS, Molloy PM, Johnson P, et al. Do Apgar scores indicate asphyxia? *Lancet* 1982; **1**(8270): 494-6.

22. Grether JK, Nelson KB. Maternal infection and cerebral palsy in infants of normal birth weight. *JAMA* 1997; **278**(3): 207-11.

23. Naeye RL. Coitus and associated amniotic-fluid infections. *N Engl J Med* 1979; **301**(22): 1198-200.

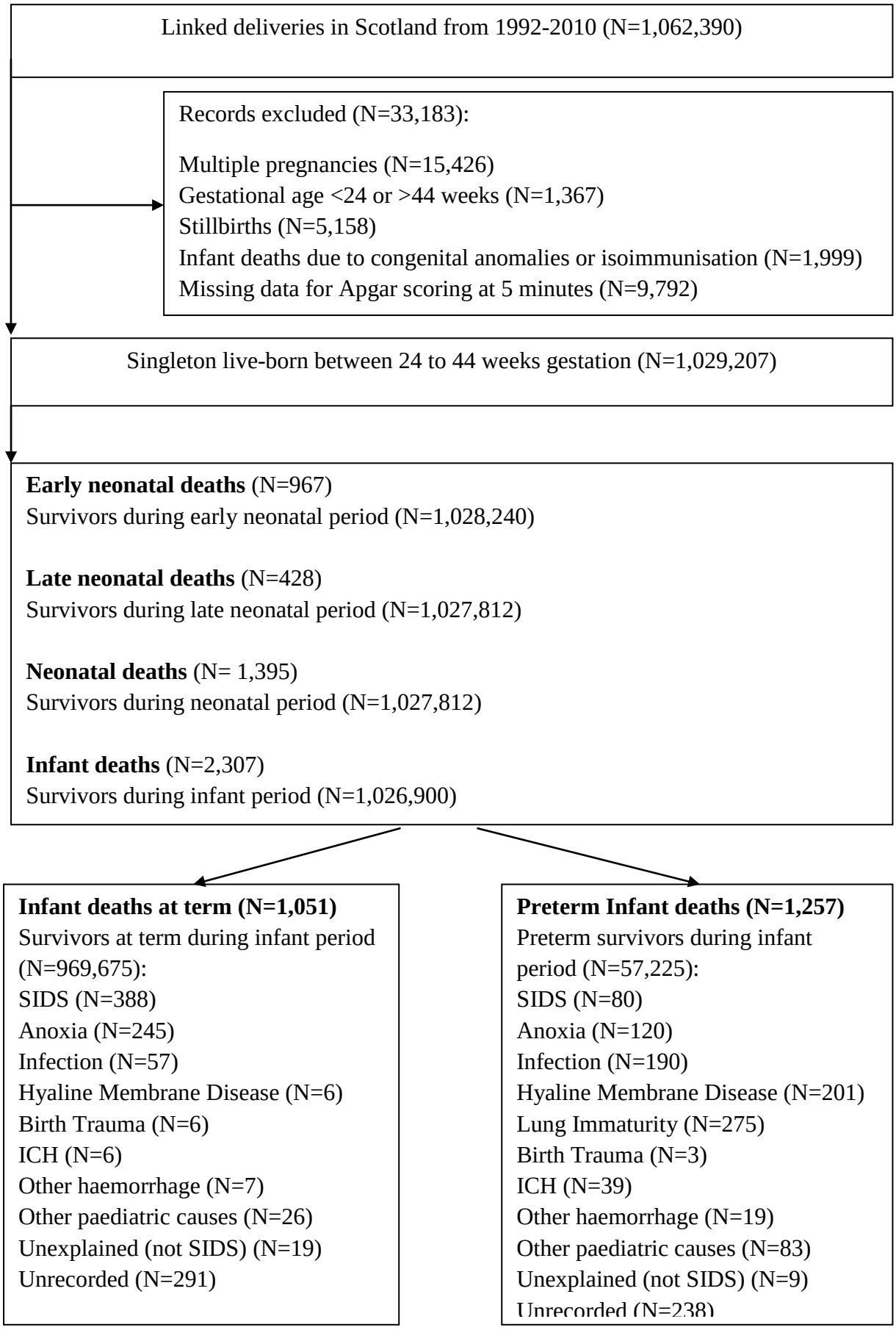
24. Buck GM, Michalek AM, Kramer AA, Batt RE. Labor and delivery events and risk of sudden infant death syndrome (SIDS). *Am J Epidemiol* 1991; **133**(9): 900-6.

25. Malloy MH. Sudden infant death syndrome among extremely preterm infants: United States 1997-1999. *J Perinatol* 2004; **24**(3): 181-7.

26. Chong DS, Yip PS, Karlberg J. Maternal smoking: an increasing unique risk factor for sudden infant death syndrome in Sweden. *Acta Paediatr* 2004; **93**(4): 471-8.

27. O'Donnell CP, Kamlin CO, Davis PG, Carlin JB, Morley CJ. Interobserver variability of the 5-minute Apgar score. *J Pediatr* 2006; **149**(4): 486-9.

Figure 1: Definition of eligible cohort and analysis sample



ICH: Intracranial haemorrhage, SIDS: Sudden infant death syndrome

Figure 2: Relative risks and 95% confidence intervals (CIs) of neonatal and infant mortality in relation to Apgar score at 5 minutes stratified per gestational age category in the complete dataset (n=1,029,207).

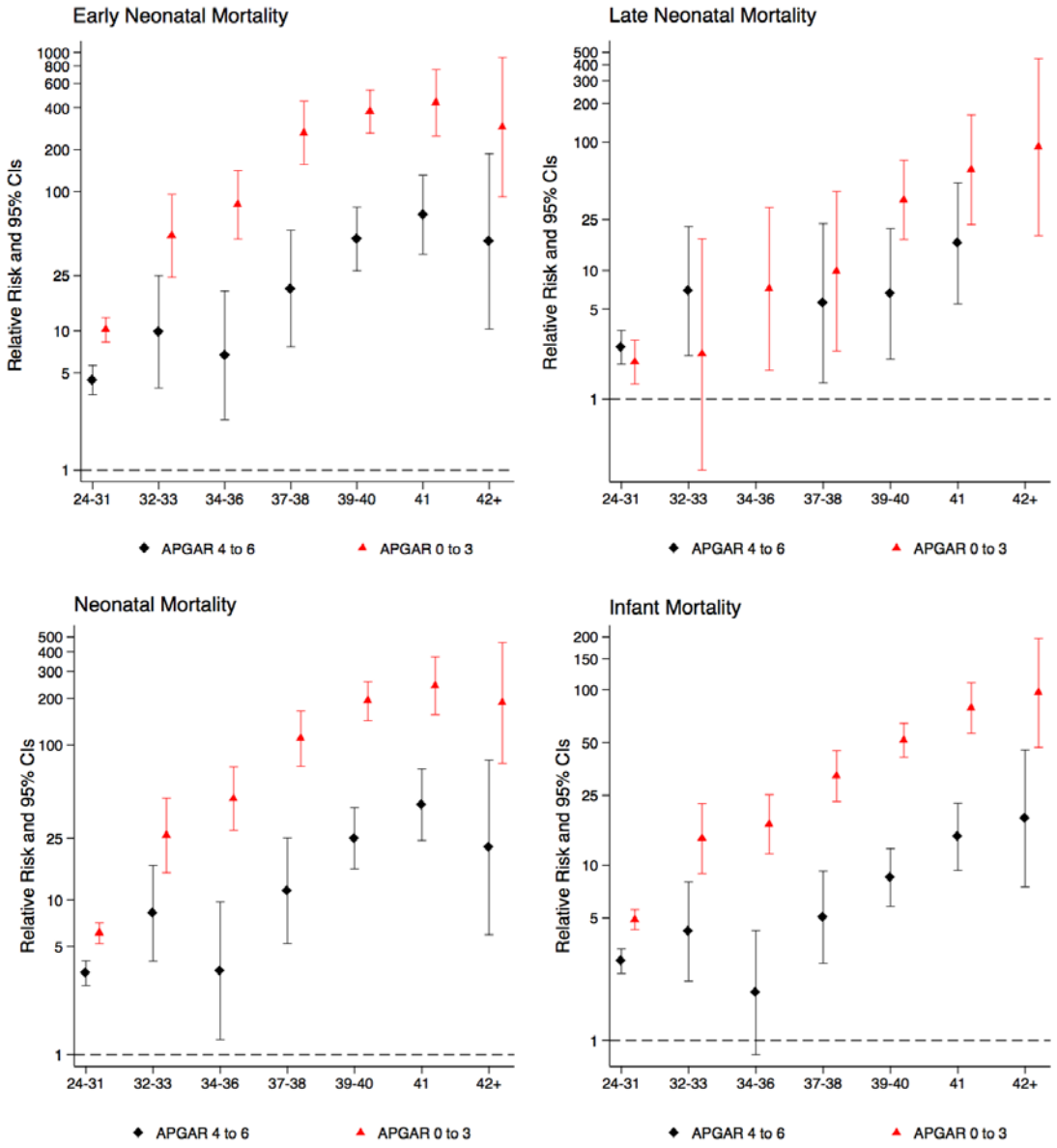


Figure 2A (top panel): Adjusted relative risks and 95% confidence intervals (CIs) of early and late neonatal mortality for neonates with low (0-3) and intermediate (4-6) Apgar score at 5 minutes referent to neonates with normal Apgar score at 5 minutes.

Figure 2B (lower panel): Adjusted relative risks and 95% confidence intervals (CIs) of neonatal and infant mortality for neonates with low (0-3) and intermediate (4-6) Apgar score at 5 minutes referent to neonates with normal Apgar score at 5 minutes.

Relative risks have been adjusted for maternal age, maternal smoking, maternal marital status, history of neonatal death, parity, Social Deprivation Score (SIMD), neonatal sex, birth-weight categories, timing and mode of delivery and year of delivery. Horizontal dashed line indicates unity

Table 1: Maternal Characteristics, delivery details and outcomes in relation to Apgar scores at 5 minutes of life (N=1,029,207).

	Apgar 7-10	**Apgar 4-6**	**Apgar 0-3**
No (%)	1,013,363 (98.46%)	10,202 (0.99%)	5,642 (0.55%)
Maternal Age (years) (IQR)	29.0 (24-33)	28 (23-32)	28.0 (24-32)
Maternal height (cm) (IQR)	163 (158-167)	162 (157-166)	162 (157-166)
Parity			
0	459,696 (45.57%)	5,604 (55.20%)	2,491 (44.29%)
1	347,324 (34.43%)	2,770 (27.29%)	1,789 (31.81%)
≥ 2	201,821 (20.01%)	1,778 (17.51%)	1,344 (23.90%)
Smoking			
Current Smokers	250,276 (27.31%)	2,825 (31.08%)	1,689 (34.62%)
Ex-smokers	86,347 (9.42%)	879 (9.67%)	452 (9.27%)
Non-smoker	579,759 (63.27%)	5,385 (59.25%)	2,737 (56.11%)
Social Deprivation Score (SIMD)			
1 (lowest social class)	144,910 (14.36%)	1,599 (15.76%)	842 (14.37)
2	120,440 (11.93%)	1,337 (13.18%)	757 (13.51%)
3	106,781 (10.58%)	1,139 (11.23%)	636 (11.35%)
4	101,291 (10.04%)	1,039 (10.24%)	588 (10.49%)
5	94,759 (9.39%)	971 (9.57%)	527 (9.40%)
6	90,325 (8.95%)	909 (8.96%)	503 (8.97%)
7	87,654 (8.68%)	873 (8.60%)	464 (8.28%)
8	88,099 (8.73%)	780 (7.69%)	440 (7.85%)
9	88,256 (8.74%)	756 (7.45%)	412 (7.35%)
10 (highest social class)	86,816 (8.60%)	743 (7.32%)	436 (7.78%)
Married	483,364 (62.66%)	4,518 (58.42%)	2,763 (60.82%)

Previous Neonatal Death			
0	839,779 (99.56%)	8,637 (99.28%)	4,151 (99.40%)
≥ 1	3,731 (0.44%)	63 (0.72%)	25 (0.60%)
Previous Stillbirth			
0	838,207 (99.37%)	8,646 (99.7%)	4,143 (99.21%)
≥ 1	5,348 (0.63%)	55 (0.63%)	33 (0.79%)
Previous miscarriage			
0	804,415 (79.40%)	8,169 (80.09%)	4,442 (78.74%)
≥ 1	208,677 (20.60%)	2,031 (19.91%)	1,199 (21.26%)
Previous termination			
0	908,666 (89.69%)	9,096 (89.69 %)	5,039 (89.33%)
≥ 1	104,437 (10.31%)	1,104 (10.82%)	602 (10.67%)
Mode of delivery			
Cephalic SVD	679,777 (69.36%)	5,224 (52.84%)	3,245 (58.47%)
Non cephalic SVD	2,767 (0.28%)	228 (2.31%)	207 (3.73%)
Instrumental delivery	90,410 (9.22%)	866 (8.76%)	378 (6.81%)
Elective Caesarean Section	80,591 (8.22%)	377 (3.81%)	249 (4.49%)
Emergency Caesarean Section	126,611 (12.92%)	3,192 (32.28%)	1,471 (26.50%)
Gestation at delivery (IQR)	40 (39-41)	39 (37-40)	39 (36-40)
Birthweight (g) (IQR)	3,420 (3,080-3,760)	3,210 (2,660-3,650)	3,130 (2,390-3,580)
Preterm	54,693 (5.40%)	2,213 (21.69%)	1,576 (27.93%)
Infant Sex			
Female	495,281 (48.88%)	4,424 (43.38%)	2,694 (47.75%)
Male	518,040 (51.52%)	5,775 (56.62%)	2,948 (52.25%)
Outcomes			

Early Neonatal Deaths (n)	316 (0.03%)	171 (1.68%)	480 (8.51%)
Late Neonatal Deaths (n)	312 (0.03%)	66 (0.65%)	50 (0.89%)
Neonatal Deaths (n)	628 (0.06%)	237 (2.32%)	530 (9.39%)
Infant Deaths (n)	1,446 (0.14%)	283 (2.77%)	578 (10.24%)

Figures are numbers (percentages) unless otherwise stated.

Abbreviations: IQR: interquartile range, NND: neonatal death, SB: stillbirth, SVD: spontaneous vaginal delivery.

Numbers (%) missing data: maternal age 10 (<0.001), maternal height 195,792 (19.02), parity 4,590 (0.45), smoking status 98,858 (9.61), SIMD 4,125 (0.40), marital status 245,510 (23.85), previous NND 172,821 (16.79), previous SB 172,775 (16.79), previous miscarriage 274 (0.03), previous termination of pregnancies 263 (0.03), mode of delivery 33,614 (3.27), gestational age 0 (0), sex 45 (<0.001), birthweight 397 (0.04).

Table 2: Crude and cause specific infant mortality rate for preterm and term infants

	Mortality rate (per 1,000 births)	Apgar 7-10	Apgar 4-6	Apgar 0-3	p-value*
Term (N=970,725)	Infant Mortality rate	8.21 (7.65, 8.80)	86.37 (67.26, 109.18)	477.3 (413.65, 547.20)	<0.001
	Infant mortality rate attributed to SIDS	4.01 (3.62, 4.43)	3.79 (0.78, 11.06)	2.58 (0.00, 14.38)	0.68
	Infant mortality rate attributed to anoxia	0.42 (0.30, 0.57)	54.00 (39.11, 72.67)	40.16 (343.11, 46.83)	<0.001
	Infant mortality rate attributed to infection	0.47 (0.34, 0.63)	3.79 (0.78, 11.06)	23.19 (10.61, 43.98)	<0.001
Preterm (N=58,482)	Infant Mortality rate	120.49 (111.51, 130.00)	967.01 (847.02, 1097.8)	2436.55 (2226.4, 2656.3)	<0.001
	Infant mortality rate attributed to SIDS	14.05 (11.07, 17.58)	9.99 (1.21, 36.06)	16.75 (20.03, 60.38)	0.97
	Infant mortality rate attributed to anoxia	4.44 (2.85, 6.61)	79.40 (45.45, 128.63)	628.93 (501.82, 776.68)	<0.001
	Infant mortality rate attributed to infection	23.08 (19.22, 27.49)	138.14 (91.98, 199.03)	301.06 (212.84, 412.60)	<0.001
	Infant mortality rate attributed hyaline membrane disease	20.50 (16.87, 24.68)	220.16 (161.03, 293.49)	363.78 (266.56, 483.76)	<0.001

Values presented as mortality per 10,000 births with 95% confidence intervals. SIDS: Sudden infant death syndrome
*Chi squared test for trend comparing mortality rates across Apgar categories

Supplementary Table 1: Neonatal and infant mortality per 10,000 births according to Apgar score and stratified for gestational age

	Neonatal Mortality					Infant Mortality				
		Apgar Score					Apgar Score			
Gestation	Crude Rate	7-10	4-6	0-3	P*	Crude Rate	7-10	4-6	0-3	P*
24-31^{+6}	972 (909.1, 1037.8)	528.3 (475.1, 585.5)	1737.3 (1503.6, 1991.1)	3545.7 (3220.2, 3881.4)	<0.001	1206 (1136.6, 1278)	734.6 (672.3, 800.8)	2037.2 (1787.5, 2305.1)	3918.3 (3584.9, 4259.3)	<0.001
32-33^{+6}	80.1 (61.2, 22.5)	33.4 (21.2, 50.1)	324.5 (163.1, 573.2)	948.9 (629.3, 1359.4)	<0.001	113.5 (90.7, 140.1)	66.9 (49.0, 89.1)	324.5 (163.1, 573.2)	1021.9 (689.9, 1443.0)	<0.001
34-36^{+6}	18 (14.2, 22.5)	10.9 (7.9, 14.6)	44.1 (12.0, 112.5)	595.7 (399.5, 849.5)	<0.001	40.3 (34.5, 46.8)	32.9 (27.6, 38.9)	66.2 (24.3, 143.4)	638.3 (434.8, 898.7)	<0.001
37-38^{+6}	5.9 (4.8, 7.1)	3.5 (2.7, 4.5)	43.9 (17.7, 90.2)	415.2 (292.5, 570.2)	<0.001	15.4 (13.7, 17.4)	12.8 (11.2, 14.5)	68.9 (34.5, 123.0)	461.4 (331.6, 623.0)	<0.001
39-40^{+6}	4.2 (3.6, 4.8)	2.0 (1.6, 2.4)	59.7 (37.9, 89.5)	415.7 (336.8, 506.9)	<0.001	9.8 (9.0, 10.7)	7.5 (6.8, 8.3)	75.3 (50.5, 108)	438.1 (357.1, 531.3)	<0.001
41-41^{+6}	4.6 (3.8, 5.6)	1.9 (1.3, 2.5)	99 (61.4, 150.9)	532.2 (387.8, 710.2)	<0.001	9.5 (8.2, 10.8)	6.5 (5.5, 7.7)	108.4 (66.8, 162.2)	569.3 (419.8, 752.1)	<0.001
≥ 42	5.8 (3.6, 8.8)	2.7 (1.3, 4.9)	71.4 (14.8, 207.3)	584.4 (270.7, 1080.4)	<0.001	10.8 (7.8, 14.7)	6.7 (4.3, 9.9)	142.9 (52.6, 308.3)	649.4 (315.8, 1161.7)	<0.001

Values presented as mortality per 10,000 births of that gestational age strata with 95% confidence intervals.
*Chi squared test for trend comparing mortality rates across Apgar categories

Supplementary Table 2: Unadjusted and adjusted relative risks of neonatal and infant mortality in relation to Apgar score

		Early Neonatal Mortality		Late Neonatal Mortality		Neonatal Mortality		Infant Mortality	
Gestation	Apgar	Unadjusted RR (95% CI)	Adjusted RR (95% CI)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Preterm	7-10	1	1	1	1	1	1	1	1
	4-6	14.28 (11.51,17.71)	14.33 (11.53, 17.82)	7.71 (5.75, 10.32)	7.34 (5.46, 9.87)	11.00 (9.29, 13.03)	10.87 (9.16, 12.89)	8.02 (6.91, 9.31)	7.83 (6.74, 9.09)
	0-3	50.46 (42.79, 59.52)	46.05 (38.87, 54.55)	7.17 (4.96, 10.39)	6.72 (4.62, 9.77)	29.47 (25.78, 33.68)	26.94 (23.49, 30.90)	20.22 (18.02, 22.70)	18.58 (16.50, 20.92)
Term	7-10	1	1	1	1	1	1	1	1
	4-6	54.53 (36.36, 81.77)	44.49 (30.81, 64.22)	11.94 (5.77, 24.7)	8.71 (4.40, 17.25)	32.37 (23.03, 45.48)	24.95 (18.32, 33.96)	11.10 (8.36, 14.73)	8.81 (6.81, 11.40)
	0-3	369.8 (274.9, 497.5)	359.4 (277.3, 465.9)	45.48 (25.34, 81.60)	30.47 (17.99, 51.62)	200.3 (157.9, 254.2)	177.8 (145.0, 218.0)	59.35 (49.02, 71.85)	50.23 (42.77, 58.98)
Gestational age categories									
24-31^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	4.22 (3.38, 5.27)	4.44 (3.48, 5.66)	2.45 (1.81, 3.32)	2.52 (1.86, 3.42)	3.29 (2.77, 3.91)	3.36 (2.79, 4.04)	2.77 (2.38, 3.22)	2.83 (2.42,3.32)
	0-3	11.34 (9.53, 13.50)	10.16 (8.31, 12.43)	2.02 (1.37, 2.97)	1.94 (1.31, 2.86)	6.71 (5.85, 7.70)	6.10 (5.23, 7.11)	5.33 (4.73, 6.02)	4.88 (4.29,5.57)
32-33^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	11.84 (4.69, 29.87)	9.85 (3.89, 24.93)	7.52 (2.41, 23.50)	6.92 (2.17, 22.06)	9.70 (4.77, 19.74)	8.20 (4.02, 16.75)	4.85 (2.54, 9.28)	4.18 (2.18,8.03)
	0-3	52.30 (26.56, 103.0)	48.11 (24.26, 95.40)	2.51 (0.32, 19.34)	2.23 (0.28, 17.57)	28.38 (16.41, 49.09)	26.05 (14.96, 45.37)	15.28 (9.70, 24.06)	14.19 (8.96, 22.46)
34-36^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	7.92 (2.75, 22.86)	6.67 (2.30, 19.35)	-	-	6.28 (1.87, 21.08)	3.47 (1.25, 9.68)	2.01 (0.89, 4.54)	1.87 (0.83, 4.23)
	0-3	99.38 (57.13, 172.9)	80.27 (45.59, 141.3)	8.46 (1.99, 35.85)	7.18 (1.67, 30.88)	46.25 (21.96, 97.42)	45.08 (28.10, 72.31)	19.39 (13.20, 28.49)	17.07 (11.58, 25.18)
37-38^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	22.08 (8.47, 57.62)	20.12 (7.67, 52.79)	5.99 (1.40, 24.82)	5.57 (1.34, 23.20)	12.47 (5.72, 27.20)	11.47 (5.24, 25.11)	5.40 (2.95, 9.87)	5.04 (2.75, 9.22)
	0-3	276.5 (165.7, 461.3)	262.6 (156.6, 445.4)	11.43 (2.76, 47.36)	9.87 (2.37, 41.17)	118.0 (78.70, 177.0)	110.2 (72.94, 166.4)	36.14 (25.99, 50.25)	32.21 (23.05, 45.00)
39-40^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	56.20 (33.39, 94.60)	45.62 (26.97, 77.17)	7.40 (2.31, 23.63)	6.60 (2.05, 21.22)	36.53 (20.62, 64.72)	24.97 (15.84, 39.37)	10.03 (6.89,14.61)	8.51 (5.82,12.42)
	0-3	406.37 (285.7, 577.9)	376.3 (262.8, 538.7)	39.47 (19.54, 79.77)	35.39 (17.41,71.93)	183.1 (119.3, 281.0)	193.1 (143.9, 256.3)	58.35 (46.94,72.53)	51.57 (41.30, 64.40)
41-41^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	90.41 (47.43, 172.4)	68.21 (35.44-131.3)	29.24 (8.88, 96.23)	16.28 (5.52, 48.01)	53.18 (31.55-89.64)	41.12(24.18, 69.91)	16.64 (10.75,25.77)	14.50 (9.31,22.58)
	0-3	530.8 (310.2, 908.1)	434.5 (250.9, 752.3)	138.9 (46.86, 411.9)	60.95 (22.81,162.8)	286.0 (188.0, 435.1)	241.9 (157.6, 371.8)	87.41 (63.23, 120.8)	78.68 (56.58,109.4)
≥42	7-10	1	1	1	1	1	1	1	1
	4-6	53.24 (12.76, 222.0)	43.98 (10.32, 187.4)	-	-	26.62 (7.35, 96.37)	21.80 (5.95,79.89)	21.3(8.78,51.64)	18.48 (7.52,45.39)
	0-3	338.8 (108.7, 1055.8)	290.2 (91.70, 918.6)	101.39 (19.83, 518.4)	91.27 (18.70,445.5)	217.8 (89.75, 528.6)	187.4 (76.42, 459.6./)	96.79 (47.3, 198.1)	96.00 (46.83, 196.8)

RR (95% CI): Relative risk with 95% confidence intervals

Horizontal bar (-) suggests small or nil number of events to specific strata so the RR is close to zero or not calculable.

Adjusted for maternal age, parity; socioeconomic deprivation; year of delivery, marital status, smoking status, previous history of neonatal death, previous history of miscarriage, previous history of termination of pregnancy; mode of delivery, and urgency of delivery, offspring sex and birthweight centile

The analysis was performed in the complete dataset with imputed values for missing values of confounders (n=1,029,207).

Supplementary Table 3: Unadjusted and adjusted relative risks of neonatal and infant mortality in relation to Apgar score in the complete dataset without missing values for confounders (n= 540,974)

		Early Neonatal Mortality		Late Neonatal Mortality		Neonatal Mortality		Infant Death Mortality	
Gestation	Apgar	Unadjusted RR (95% CI)	Adjusted RR (95% CI)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Preterm	7-10	1	1	1	1	1	1	1	1
	4-6	16.48 (12.09, 22.46)	17.14 (12.56, 23.39)	8.34 (5.37, 12.96)	8.05 (5.15, 12.58)	12.55 (9.80, 16.06)	12.78 (9.97, 16.37)	9.07 (7.31, 11.25)	9.10 (7.33, 11.31)
	0-3	50.28 (39.28, 64.35)	47.79 (37.26, 61.30)	9.10 (5.44, 15.22)	8.80 (5.24, 14.77)	30.71 (25.11, 37.56)	29.20 (23.83, 35.76)	20.43 (17.14, 24.35)	19.42 (16.30, 23.17)
Term	7-10	1	1	1	1	1	1	1	1
	4-6	68.45 (43.29, 108.2)	57.10 (35.94, 90.72)	16.94 (8.07, 35.54)	13.84 (6.55, 29.24)	41.15 (28.31, 59.81)	34.16 (23.41, 49.86)	13.32 (9.77, 18.17)	11.81 (8.64, 16.15)
	0-3	403.3 (282.7, 575.4)	361.2 (252.2, 517.3)	48.65 (24.84, 95.28)	41.54 (21.11, 81.73)	214.7 (162.1, 284.4)	188.4 (141.7, 250.5)	61.82 (49.46, 77.26)	55.14 (44.03, 69.06)
Gestational age categories									
24-31^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	4.36 (3.16, 6.02)	4.38 (3.19, 6.02)	2.74 (1.74, 4.31)	2.78 (1.77, 4.37)	3.54 (2.75, 4.55)	3.64 (2.77, 4.78)	2.90 (2.33, 3.62)	2.92 (2.35, 3.63)
	0-3	10.24 (7.90, 13.26)	8.79 (6.79, 11.38)	2.57 (1.51, 4.37)	2.52 (1.49, 4.27)	6.60 (5.36, 8.14)	5.88 (4.69, 7.36)	4.96 (4.12, 5.96)	4.42 (3.67, 5.31)
32-33^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	19.51 (5.29, 71.89)	16.35 (4.46, 59.99)	3.13 (0.39, 24.85)	2.37 (0.30, 18.86)	9.38 (3.39, 25.96)	7.58 (2.75, 20.91)	5.30 (2.04,13.75)	4.12 (1.59, 10.66)
	0-3	64.73 (23.39, 179.1)	66.77 (23.84, 187.0)	-	-	24.90(11.76, 52.72)	23.37 (10.97, 49.80)	15.15 (7.97, 28.83)	13.02 (6.80, 24.95)
34-36^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	14.22 (3.93, 51.50)	13.27 (3.64, 48.41)	-	-	6.77 (2.03, 22.62)	6.33 (1.88, 21.25)	3.11 (1.14, 8.51)	3.12 (1.14, 8.54)
	0-3	89.75 (36.83, 218.7)	86.52 (35.23, 212.5)	9.44 (1.22, 72.83)	9.21 (1.17, 72.28)	47.49 (22.63, 99.66)	45.46 (21.55, 95.89)	17.98 (9.59, 33.71)	16.31 (8.65, 30.76)
37-38^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	16.26 (4.82, 54.83)	15.21 (4.48, 51.65)	10.33 (2.42, 44.12)	8.61 (2.00, 37.11)	13.20 (5.21, 33.41)	11.83 (4.65, 30.08)	6.49 (3.18,13.21)	6.05 (2.97, 12.36)
	0-3	195.7 (102.4, 373.8)	184.1 (95.98, 353.1)	-	-	95.32 (54.37, 167.1)	86.91 (49.37, 153.0)	29.27 (17.81, 48.12)	27.01(16.36, 44.60)
39-40^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	82.17 (42.10, 160.4)	68.17 (34.68, 134.0)	10.40 (2.46, 43.87)	8.58 (2.02, 36.51)	43.96 (24.97, 77.39)	36.53 (20.62, 64.73)	13.48 (8.42, 21.58)	11.30 (7.03, 18.16)
	0-3	384.2 (224.8, 656.8)	347.3 (202.0, 597.1)	52.88 (20.28, 137.9)	47.12 (17.98, 123.5)	207.1 (135.6, 316.2)	182.9 (119.2, 280.7)	57.71 (41.35, 80.54)	49.92 (35.65, 69.89)
41-41^{+6}	7-10	1	1	1	1	1	1	1	1
	4-6	152.2 (62.34, 371.7)	121.9 (49.44, 300.5)	41.00 (12.88, 130.6)	30.84 (9.45, 100.7)	90.21 (46.11, 176.5)	70.97 (35.94, 140.2)	23.63 (13.98, 39.94)	21.50 (12.64, 36.57)
	0-3	1002.3 (458.1, 2193.0)	846.5 (383.4, 1869.2)	159.0 (54.61, 463.0)	136.5 (46.01, 404.7)	528.0 (298.8, 932.9)	446.4 (250.7, 794.7)	138.3 (93.17, 205.4)	130.3 (87.16, 194.7)
≥ 42	7-10	1	1	1	1	1	1	1	1
	4-6	22.38 (2.51, 199.5)	28.53 (3.08, 263.9)	-	-	12.79 (1.58, 103.5)	11.26 (1.35, 94.05)	11.94 (2.75, 51.90)	11.11 (2.53, 48.82)
	0-3	232.0 (58.95, 912.9)	199.6 (50.72, 785.6)	80.99 (8.51, 770.7)	75.02 (7.16, 785.9)	165.7 (53.61, 512.1)	161.8 (53.98, 485.1)	92.79 (36.86, 233.6)	90.58 (38.18, 214.9)

RR (95% CI): Relative risk with 95% confidence intervals

Horizontal bar (-) suggests small or nil number of events to specific strata so the RR is close to zero or not calculable.

Adjusted for maternal age, parity; socioeconomic deprivation; year of delivery, marital status, smoking status, previous history of neonatal death, previous history of miscarriage, previous history of termination of pregnancy; mode of delivery, and urgency of delivery, offspring sex and birthweight centile

Supplementary Table 4: Risk factors independent of Apgar score category for neonatal and infant mortality in term and preterm neonates

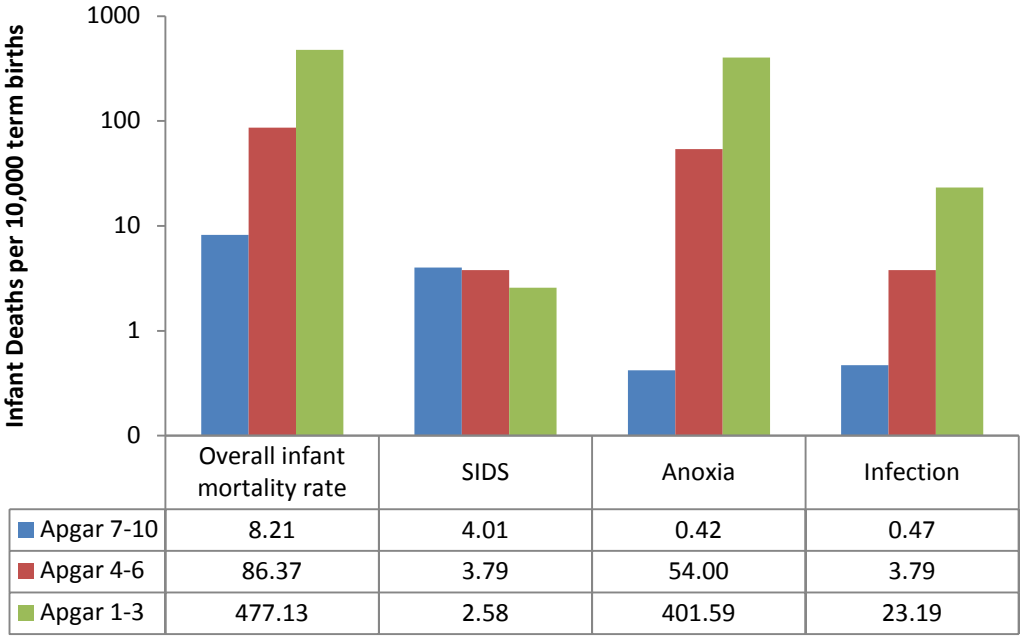
		Early Neonatal Mortality		Late Neonatal Mortality		Infant Mortality	
Gestation	Co-variates	Adjusted RR (95% CI)	p-value	Adjusted RR (95% CI)	p-value	Adjusted RR (95% CI)	p-value
Preterm	Maternal age (per one year increase)	0.99 (0.97-1.01)	0.52	0.97 (0.94-1.00)	0.08	0.98 (0.97-0.99)	**0.02**
	Former or never smokers	1		1		1	
	Current smokers	1.18 (0.93-1.50)	0.16	0.94 (0.64-1.38)	0.74	1.16 (0.97-1.37)	0.10
	SIMD (per one decile increase from most deprived to least deprived areas)	0.96 (0.92-1.00)	**0.05**	0.94 (0.88-1.01)	0.10	0.96 (0.93-0.99)	**0.006**
	Not currently married	1		1		1	
	Married	1.26 (0.98-1.63)	0.08	1.04 (0.68-1.59)	0.85	1.15 (0.95-1.39)	0.14
	Nulli-parity	1		1		1	
	Parity	0.87 (0.66-1.15)	0.32	1.19 (0.79-1.79)	0.41	1.00 (0.83-1.22)	0.97
	No history of NND	1		1		1	
	History of NND	2.09 (1.01-4.34)	**0.05**	1.88 (0.58-6.05)	0.29	1.75 (1.01-3.06)	**0.05**
	Abdominal delivery	1		1		1	
	Vaginal delivery	0.92 (0.69-1.22)	0.55	0.72 (0.46-1.14)	0.16	0.90 (0.73-1.10)	0.30
	Unplanned delivery	1		1		1	
	Planned delivery	0.60 (0.45-0.80)	**0.001**	0.61 (0.39-0.97)	**0.04**	0.72 (0.59-0.89)	**0.002**
	Birthweight 11^{th} -90^{th} centile	1		1		1	
	Birthweight ≤ 10^{th} centile	0.94 (0.64-1.37)	0.73	1.22 (0.69-2.16)	0.49	1.05 (0.81-1.37)	0.72
	Birthweight >90^{th} centile	1.22 (0.85-1.75)	0.27	0.91 (0.48-1.75)	0.79	1.03 (0.78-1.37)	0.84
	Female gender	1		1		1	
	Male gender	1.07 (0.93-0.98)	0.55	1.58 (1.10-2.28)	**0.01**	1.20 (1.02-1.41)	**0.02**
	Year of delivery (per one year increase)	0.96 (0.93-0.98)	**<0.001**	0.98 (0.95-1.02)	0.32	0.97 (0.96-0.99)	**0.002**

Term	Maternal age (per one year increase)	1.02 (0.99-1.06)	0.11	0.92 (0.88-0.97)	**0.004**	0.96 (0.95-0.98)	**<0.001**
	Former or never smokers	1		1		1	
	Current smokers	0.66 (0.43-1.00)	**0.05**	1.27 (0.76-2.10)	0.36	1.68 (1.39-2.03)	**<0.001**
	SIMD (per one decile increase from most deprived to least deprived areas)	0.95 (0.90-1.01)	0.10	0.91 (0.83-1.00)	0.06	0.94 (0.91-0.98)	**0.001**
	Not currently married	1		1		1	
	Married	1.18 (0.81-1.73)	0.39	1.20 (0.68-2.13)	0.52	0.88 (0.72-1.09)	0.25
	Nulli-parity	1		1		1	
	Parity	0.57 (0.39-0.85)	**0.006**	1.58 (0.89-2.79)	0.12	1.40 (1.14-1.72)	**0.001**
	No history of NND	1		1		1	
	History of NND	1.83 (0.25-13.31)	0.55	2.84 (0.38-21.00)	0.31	3.14 (1.61-6.12)	**0.001**
	Abdominal delivery	1		1		1	
	Vaginal delivery	0.37 (0.26-0.52)	**<0.001**	0.67 (0.38-1.16)	0.15	0.62 (0.50-0.77)	**<0.001**
	Planned delivery	1		1		1	
	Planned delivery	0.88 (0.63-1.24)	0.49	1.66 (1.01-2.71)	**0.045**	0.98 (0.81-1.19)	0.85
	Birthweight 11^{th}-90^{th} centile	1		1		1	
	Birthweight $\leq 10^{th}$ centile	1.17 (0.76-1.80)	0.49	2.15 (1.26-3.66)	**0.005**	1.59 (1.28-1.97)	**<0.001**
	Birthweight $>90^{th}$ centile	0.91 (0.52-1.58)	0.73	0.17 (0.021.26)	0.08	0.60 (0.40-0.90)	**0.01**
	Female gender	1		1		1	
	Male gender	0.77 (0.57-1.05)	0.10	1.00 (0.64-1.59)	0.98	1.10 (0.93-1.31)	0.28
	Year of delivery (per one year increase)	0.99 (0.96-1.02)	0.59	0.93 (0.89-0.99)	**0.02**	0.98 (0.96-0.99)	**0.03**

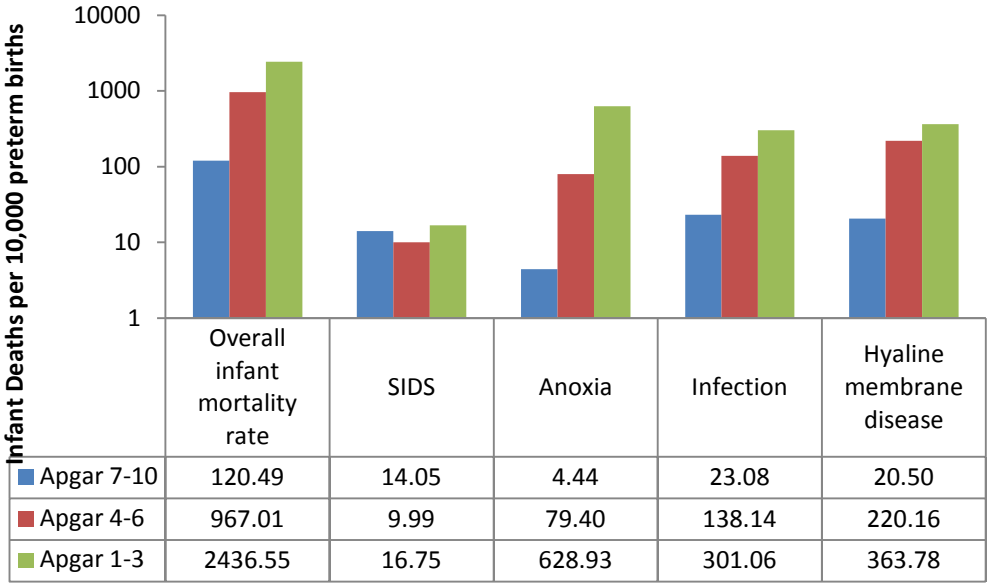
The relative risks (RR) and 95% confidence intervals (CIs) are adjusted for all the above factors with additional adjustment for Apgar score category at 5 minutes.

SIMD; Scottish Index of Multiple Deprivation, NND: neonatal death.

Supplementary Figure 1: Crude and cause specific infant mortality rate for term and preterm infants



	Overall infant mortality rate	SIDS	Anoxia	Infection
Apgar 7-10	8.21	4.01	0.42	0.47
Apgar 4-6	86.37	3.79	54.00	3.79
Apgar 1-3	477.13	2.58	401.59	23.19



	Overall infant mortality rate	SIDS	Anoxia	Infection	Hyaline membrane disease
Apgar 7-10	120.49	14.05	4.44	23.08	20.50
Apgar 4-6	967.01	9.99	79.40	138.14	220.16
Apgar 1-3	2436.55	16.75	628.93	301.06	363.78

Figure 1A (top panel): Overall and cause specific infant mortality for term infants (N=970,725). Expressed as number of deaths per 10,000 term births utilising a $\log_{10}$ scale.

Figure 1B (lower panel): Overall and cause specific infant mortality for preterm infants (N=58,482). Expressed as number of deaths per 10,000 term births utilising a $\log_{10}$ scale.

SIDS: Sudden infant death syndrome