

## Time of birth and risk of neonatal death at term: retrospective cohort study

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### ABSTRACT

**Objective** To determine the effect of time and day of birth on the risk of neonatal death at term.

**Design** Population based retrospective cohort study.

**Setting** Data from the linked Scottish morbidity records, Stillbirth and Infant Death Survey, and birth certificate database of live births in Scotland, 1985-2004.

**Subjects** Liveborn term singletons with cephalic presentation. Perinatal deaths from congenital anomalies excluded. Final sample comprised 1 039 560 live births.

**Main outcome measure** All neonatal deaths (in the first four weeks of life) unrelated to congenital abnormality, plus a subgroup of deaths ascribed to intrapartum anoxia.

**Results** The risk of neonatal death was 4.2 per 10 000 during the normal working week (Monday to Friday, 0900-1700) and 5.6 per 10 000 at all other times (out of hours) (unadjusted odds ratio 1.3, 95% confidence interval 1.1 to 1.6). Adjustment for maternal characteristics had no material effect. The higher rate of death out of hours was because of an increased risk of death ascribed to intrapartum anoxia (adjusted odds ratio 1.7, 1.2 to 2.3). Though exclusion of elective caesarean deliveries attenuated the association between death ascribed to anoxia and delivery out of hours, a significant association persisted (adjusted odds ratio 1.5, 1.1 to 2.0). The attributable fraction of neonatal deaths ascribed to intrapartum anoxia associated with delivery out of hours was 26% (95% confidence interval 5% to 42%).

**Conclusions** Delivering an infant outside the normal working week was associated with an increased risk of neonatal death at term ascribed to intrapartum anoxia.

### INTRODUCTION

Many previous studies have sought to determine whether the risk of perinatal mortality varies in relation to the time and day of birth.<sup>1-12</sup> The motivation for these studies has been to determine whether possible variations in the care provided to women in labour could be reflected in variation in important adverse outcomes. The question is of practical relevance to the planning of obstetric care as considerable variation in the risk of death outside the normal working week would indicate that improvements in the level of

clinical services provided out of hours might be an effective strategy in reducing rates of perinatal death. The findings of previous studies, however, have been inconsistent, with some reporting increased rates of perinatal death at the weekend<sup>5-7</sup> and at night,<sup>2-4 10-12</sup> whereas others have found no difference after adjustment for birth weight.<sup>1 8 9</sup>

The inconsistent nature of previous findings could reflect the underlying complexity of adequately examining this question. The provision of care, in particular the provision of facilities to allow rapid delivery and prompt resuscitation, would be expected to affect different types of death in different ways. These provisions might be crucial in the response to an acute event, such as uterine rupture. They would not, however, alter the course of a baby affected by renal agenesis, which is invariably fatal.<sup>13</sup> Furthermore, there is considerable potential for bias within any such analysis. Planned caesarean delivery at term carries a low risk of neonatal death<sup>14-16</sup> and tends to be performed during the normal working week. Hence, inclusion of such cases would lead to an overestimate of the risk of delivering out of hours. Conversely, high risk deliveries, such as elective preterm birth, also usually conducted during the working week, could lead to an underestimate of the relative risk of delivering out of hours. Finally, perinatal death is a rare event, and informative analyses require a large sample size. To examine this question, a data source is required that combines relatively detailed information on the cause of perinatal death with detailed information on the obstetric characteristics of babies who died and survivors for a large number of births. We used a linkage of Scottish national registries of perinatal deaths and births.

### METHODS

#### Data

The Scottish morbidity record (SMR02) collects information on clinical and demographic characteristics and outcomes for all patients discharged from Scottish maternity hospitals. The register is subjected to regular quality assurance checks and since the late 1970s has been more than 99% complete.<sup>17</sup> A quality assurance exercise was conducted in 1996-7 in which 5% of case

**Table 1** Characteristic of cohort by timing of birth, Scotland 1985-2004. Figures are numbers (percentages) unless stated otherwise

Characteristics	Timing of birth		P value*
	Monday to Friday 0900-1700 (n=287 545, 27.7%)	Births at all other times (n=752 015, 72.3%)	
<b>Maternal</b>			
Median (IQR) age (years)†	28 (24-32)	27 (23-31)	<0.001
Parity†:			
0	112 597 (39.2)	347 205 (46.1)	
1-2	155 126 (54.0)	357 657 (47.6)	<0.001
>2	19 704 (6.8)	47 903 (6.4)	
Median (IQR) height (cm)†	162 (157-166)	162 (157-167)	<0.001
Socioeconomic status†:			
1 (least deprived)	16 781 (5.9)	41 745 (5.6)	
2	37 276 (13.1)	99 208 (13.4)	
3	58 263 (20.5)	154 606 (20.8)	
4	68 655 (24.2)	181 982 (24.5)	<0.001
5	44 470 (15.7)	117 442 (15.8)	
6	35 166 (12.4)	87 892 (11.8)	
7 (most deprived)	23 371 (8.2)	59 670 (8.0)	
<b>Fetal</b>			
Median (IQR) gestation (weeks)	40 (39-40)	40 (39-41)	<0.001
Median (IQR) birth weight (g)†	3440 (3120-3760)	3440 (3120-3760)	0.05
Male†	146 998 (51.1)	385 453 (51.3)	0.22
<b>Obstetric and service</b>			
Onset of labour†:			
Spontaneous	223 141 (77.6)	556 845 (74.1)	<0.001
Non-prostaglandin induction	30 870 (10.7)	82 068 (10.9)	0.01
Prostaglandin induction	33 457 (11.6)	112 839 (15.0)	<0.001
Mode of delivery:			
Spontaneous vaginal	194 393 (67.6)	583 701 (77.6)	<0.001
Assisted vaginal	31 689 (11.0)	99 036 (13.2)	<0.001
Emergency caesarean	21 153 (7.4)	66 743 (8.9)	<0.001
Elective caesarean	40 310 (14.0)	2 535 (0.3)	<0.001
Hospital throughput (births/year):			
<1000	19 920 (6.9)	58 373 (7.8)	
1000-1999	57 603 (20.0)	155 325 (20.7)	
2000-2999	64 873 (22.6)	161 137 (21.4)	<0.001
3000-3999	67 209 (23.4)	167 237 (22.2)	
≥4000	77 940 (27.1)	209 343 (27.9)	

IQR=interquartile range.

\* $\chi^2$  test or Mann-Whitney U test as appropriate.

†Missing data: maternal age 19 (0.002%); parity 368 (0.04%); height 129 601 (12.5%); socioeconomic deprivation 13 033 (1.3%), birth weight 311 (0.03%), fetal sex 23 (0.002%), and onset of labour 340 (0.03%).

records (n=1414) were compared with the SMR02 database during a six month period. This exercise showed that all fields used in the present study had less than 2% errors with the exception of maternal height (4.4%), estimated gestation (5.6%), and induction of labour (6.4%).<sup>18</sup>

Records of singleton births from the SMR02 for 1985-2004 were identified and linked to the Scottish Stillbirth and Infant Death Survey (SSBIDS), a national registry that routinely classifies all perinatal deaths in Scotland. A single medically qualified individual (the Scottish coordinator) codes the cause of death in the Information and Statistics Division of the NHS on the basis of the clinical information obtained from the local coordinators and pathologists. Cases are

identified through registration of stillbirths and neonatal deaths with the General Register Office, which is a legal requirement after perinatal death. The register is 100% complete compared with the death certificate database and has been described in detail elsewhere.<sup>19,20</sup>

### Study cohort

We carried out a population based retrospective cohort study of all singleton liveborn infants in a cephalic presentation delivered at term in 1985-2004. Multiple pregnancy, stillbirths, perinatal death ascribed to congenital abnormality or rhesus isoimmunisation, delivery outside 37-43 weeks' gestation, records with unknown mode or time of delivery, and deliveries in units with fewer than 10 deliveries a year were all excluded.

The primary outcome was neonatal death unrelated to congenital abnormality or rhesus isoimmunisation. We also studied a subgroup of these deaths where the cause was ascribed to intrapartum anoxia. Neonatal death was defined as death during the first four weeks of life in a liveborn baby. The cause of neonatal death was coded with a modification of the Wigglesworth classification, described in detail elsewhere.<sup>19,21,22</sup> The definition of anoxia was broad, including hypoxia, acidosis, and asphyxia. Information on the time of birth was recorded with the 24 hour clock. Information on both the day and time of birth was used to classify the timing of birth into births between 0900 and 1700 Monday to Friday, births between 1701 Monday to Friday and 0859 the following day, and births from 0900 on a weekend to 0859 the next day. Collectively, out of hours births were defined as all births at any time other than 0900-1700, Monday to Friday.

We adjusted the risk of neonatal death for year of birth; maternal age, height, and parity; socioeconomic deprivation; sex of the baby; gestational age; birth-weight centile; onset of labour; and hospital throughput. All these characteristics except the following were defined as previously described.<sup>16</sup> Onset of labour was categorised into spontaneous non-prostaglandin induction and prostaglandin induction. Operative vaginal delivery was defined as vaginal delivery with either obstetric forceps or vacuum (ventouse). Emergency caesarean delivery was defined as any caesarean that was not scheduled in advance. It also includes emergency procedures performed before the onset of labour and procedures performed because of arrested progress in labour in the absence of an urgent indication for delivery (such as fetal distress). Elective caesarean delivery was defined as procedures where the time was planned in advance. Hospital throughput was defined as the total number of births recorded in the SMR02 database for a given hospital over a given year.

### Statistical analysis

We used medians and interquartile ranges to summarise continuous variables and the Mann-Whitney U test for comparisons between groups. We used  $\chi^2$  and  $\chi^2$  for trend as appropriate for univariate comparisons of

**Table 2** | Incidence of cause specific neonatal death by day and time of birth, Scotland 1985-2004

Day of week and time of birth	No (%) of live births	Incidence of neonatal death per 10 000 (95% CI)		
		All cause	Anoxia	Not anoxia
Weekday, 0900-1700	287 545 (27.7)	4.2 (3.5 to 5.0)	1.7 (1.3 to 2.3)	2.5 (1.9 to 3.1)
Weekday, 1701-0859	491 025 (47.2)	5.5 (4.8 to 6.2)	2.9 (2.5 to 3.4)	2.6 (2.1 to 3.1)
Weekend, 0900-0859	260 990 (25.1)	5.7 (4.8 to 6.7)	3.1 (2.4 to 3.8)	2.6 (2.1 to 3.3)
All out of hours	752 015 (72.3)	5.6 (5.0 to 6.1)	3.0 (2.6 to 3.4)	2.6 (2.2 to 3.0)

dichotomous data. The risk of an event was modelled with logistic regression. Linearity of continuous variables in logistic regression models was tested with fractional polynomials. Missing covariate values were imputed with multiple imputation by chained equations.<sup>23</sup> We used a set of models constructed from all covariates and outcome variables in their raw scale to impute missing values for maternal age, height, and parity, socioeconomic deprivation status, fetal sex, birth weight, and onset of labour and created five imputations. The analysis was repeated with adjustment for clustering at the level of hospitals and individuals. The significance of interaction terms was assessed with the Wald test. All P values were two sided and the significance was set at  $P < 0.05$ . All analyses were performed with Stata, version 10.0 (StataCorp LP, College Station, TX).

## RESULTS

There were 1 163 914 records of singleton births in Scotland for 1985-2004. We excluded 69 492 (6%) records where the gestational age was outside 37-43 weeks and 3677 (0.3%) with missing values for gestational age. Of the term deliveries, we excluded 899 (0.08%) perinatal deaths ascribed to congenital abnormality or rhesus isoimmunisation, 2054 (0.2%) stillbirths, and 44 000 (4.0%) non-cephalic deliveries. We also excluded 3184 (0.3%) records with missing values for time of birth, 334 (0.03%) records with unknown mode of delivery, 717 (0.1%) records where the deliveries were documented to have taken place in hospitals with fewer than 10 deliveries a year, and five records with inconsistent classification of perinatal death. Our study cohort consisted of 1 039 560 live births (some records had multiple exclusions), which corresponded to over 95% of all singleton term births in Scotland for 1985-2004. About half of the records excluded from the study cohort were preterm births of liveborn infants without congenital abnormalities ( $n=64\,625$ , 52%). Among the study cohort, 72% of births occurred out of hours, whereas the figure was lower (70%) for preterm births over the period of study ( $P < 0.001$ ).

Women who delivered out of hours were younger, more likely to be primiparous, more likely to live in an area of low socioeconomic deprivation, and more likely to deliver in either low or high throughput units (table 1). They were more likely to have had labour induced and much less likely to be delivered by planned caesarean section. Their infants were also born at later gestational ages.

There were 539 (0.05%) neonatal deaths in the study cohort (5.2 per 10 000 live births, 95% confidence interval 4.8 to 5.6). About half of these deaths were ascribed to intrapartum anoxia ( $n=273$ , 51%). The risk of neonatal death was 4.2 per 10 000 live births (3.5 to 5.0) during the working week and higher at all other times (table 2). The higher rate of neonatal death out of hours was explained by a significant excess risk of death ascribed to anoxia (unadjusted odds ratio 1.7, 1.3 to 2.3) and was similar in multivariable analysis. The magnitude (adjusted odds ratio of the increased risk of anoxic death was similar when we compared both 1701-0859 Monday to Friday (1.6, 1.2 to 2.2) and the weekends (1.7, 1.2 to 2.5) (table 3). When we stratified data by weekday or weekend, delivery between 1701 and 0859 was associated with an increased risk of anoxic death on weekdays (1.7, 1.2 to 2.3) but not at the weekend (0.7, 0.5 to 1.2) (interaction term  $P=0.005$ ). When we excluded elective caesarean deliveries from the analysis, the association between timing of birth and the risk of neonatal death ascribed to anoxia was attenuated (table 3), but a significant association persisted. Similarly, the interaction between time of birth and day of the week was still present after we excluded elective caesarean births (interaction term  $P=0.01$ ).

There was no evidence that the association between delivery out of hours and the risk of neonatal death ascribed to anoxia significantly varied over the study period (interaction term  $P=0.50$ ); in relation to hospital throughput (interaction term  $P=0.23$ ); for women who had a spontaneous labour compared with those in whom labour was induced (interaction term  $P=0.91$ ); or for spontaneous vaginal deliveries compared with operative vaginal and emergency caesarean deliveries (interaction term  $P=0.73$ ). After exclusion of births by elective caesarean section, the attributable fraction of neonatal deaths associated with delivery out of hours was 16.5% (1.3% to 29.3%) for deaths from all causes and 25.9% (4.8% to 42.3%) for neonatal deaths attributed to intrapartum anoxia. The nature of associations between delivery out of hours and the risk of neonatal death were unaffected when we performed clustered analyses accounting for births within hospitals (hospital level) or repeated deliveries in the same individual (maternal level).

## DISCUSSION

The risk of neonatal death was higher among women who delivered outside the hours of the normal working week. The excess risk was similar for births between

**Table 3** | Unadjusted and adjusted odds ratios (95% confidence interval) for cause specific neonatal death by day and time of birth

Timing of birth	Unadjusted			Adjusted*			Adjusted* (excluding elective caesarean†)		
	All cause	Anoxia	Not anoxia	All cause	Anoxia	Not anoxia	All cause	Anoxia	Not anoxia
Weekday, 0900-1700	(1.0)	(1.0)	(1.0)	(1.0)	(1.0)	(1.0)	(1.0)	(1.0)	(1.0)
Weekday, 1701-0859	1.3‡ (1.1 to 1.6)	1.7§ (1.2 to 2.3)	1.0 (0.8 to 1.4)	1.3‡ (1.0 to 1.6)	1.6§ (1.2 to 2.2)	1.1 (0.8 to 1.4)	1.2 (0.9 to 1.5)	1.4‡ (1.0 to 1.9)	1.1 (0.8 to 1.5)
Weekend	1.4‡ (1.1 to 1.7)	1.8§ (1.2 to 2.5)	1.1 (0.8 to 1.5)	1.4‡ (1.1 to 1.7)	1.7§ (1.2 to 2.5)	1.1 (0.8 to 1.5)	1.3‡ (1.0 to 1.7)	1.5‡ (1.1 to 2.1)	1.1 (0.8 to 1.6)
All out of hours	1.3§ (1.1 to 1.6)	1.7§ (1.3 to 2.3)	1.1 (0.8 to 1.4)	1.3‡ (1.1 to 1.6)	1.7§ (1.2 to 2.3)	1.1 (0.8 to 1.4)	1.3 (1.0 to 1.6)	1.5‡ (1.1 to 1.9)	1.1 (0.8 to 1.5)

\*Adjusted for year of delivery, maternal age, parity, height, socioeconomic deprivation, gestational age, birthweight centile, fetal sex, onset of labour, and hospital throughput.

†After exclusion of deliveries by elective caesarean, unadjusted odds ratio for all out of hours births was 1.3 (1.0 to 1.6) for all cause death, 1.5 (1.1 to 2.0) for anoxic death, and 1.1 (0.8 to 1.5) for non-anoxic death.

‡P<0.05.

§P<0.01.

1701 and 0859 Monday to Friday and births at the weekend. This observation was explained by about a 70% increase in the risk of neonatal death ascribed to anoxia. Births during the normal working week, however, included a much higher proportion of planned caesarean deliveries, which are associated with extremely low rates of neonatal death from anoxia.<sup>14-16</sup> Nevertheless, after exclusion of planned caesarean delivery, birth out of hours was still associated with about a 45% increased risk of death ascribed to anoxia. The association was not explained by a confounding effect of measured maternal, infant, and obstetric characteristics. The association did not vary significantly over the study period in relation to hospital throughput or in relation to the onset of labour or the eventual mode of delivery. If we assume causality, the increased risk of delivering out of hours accounted for about a quarter of all neonatal deaths at term ascribed to intrapartum anoxia.

#### Results in context

The association between delivery out of hours and neonatal death ascribed to intrapartum anoxia could be a result of many different variables. Epidemiological studies of this type have limited capacity to identify the causal pathways leading to observed associations. For example, it could be explained by variation in staffing at different times of day, such as the total number of staff or the profile of staff, in particular the immediate availability of senior clinicians. It could also be related to access to clinical facilities, such as obstetric operating theatres. We lacked data to evaluate the effect of any of these factors on the observed association, and our findings might reflect multiple characteristics of delivery out of hours. Fatigue among clinical staff is often suggested as a cause of increased risk of adverse outcomes observed at night.<sup>2</sup> This is unlikely to explain our findings as there was no excess risk of death among women delivering during the night compared with the daytime at the weekends.

#### Other studies

Previous studies have examined the relation between time and day of birth and the risk of perinatal death. There have been no consistent results, possibly

reflecting the intrinsic difficulties in studying this question. Several studies simply compared the risk of death on weekend days compared with weekdays, without reference to the time of birth.<sup>15-8</sup> This ignores the fact that most births on weekdays also occur out of normal working hours. Therefore, the comparator group includes a considerable proportion of births where the same issues of reduced provision of clinical care apply as at weekends. Conversely, some studies considered only the time of birth, ignoring differences between weekdays and the weekend.<sup>2-4,9,10</sup> Some of the studies lacked the necessary information to exclude births by planned caesarean delivery.<sup>12,4-10</sup> As discussed above, this could lead to an apparent increase in the risk of out of hours delivery. Several studies included stillbirths.<sup>5,6,8-10</sup> In most stillbirths, however, the fetus dies before the onset of labour<sup>24</sup> so the facilities available for intrapartum care out of hours cannot directly influence rates of these events. Moreover, even when intrapartum stillbirth can be reliably identified, it does not follow that the timing of death and the timing of delivery were closely correlated. Finally, several studies pooled perinatal death ascribed to multiple different causes.<sup>1,6-11</sup> Our results indicate that the association between death out of hours is explained by an increased risk of death from anoxia but not other causes. Inclusion of deaths from other causes, which are less likely to be significantly determined by the out of hours facilities available, might mask the association. This association probably also occurs in other countries, such as the United States, where rates of neonatal death at term, excluding losses from congenital abnormality, are similar (about five per 10 000<sup>25</sup>) to those in the present study (5.2 per 10 000 live births).

#### Conclusion

Improving the level of clinical care for women delivering out of normal working hours might reduce overall rates of perinatal death. The absolute risk of neonatal death ascribed to intrapartum anoxia among women delivering out of hours was relatively small, in the region of three to four per 10 000. Though the increased risk among women delivering out of hours accounts for a significant proportion of these losses, the necessary expenditure to reduce the risk of these

**WHAT IS ALREADY KNOWN ON THIS TOPIC**

Perinatal death ascribed to intrapartum anoxia at term is regarded as a sensitive measure of care during labour and delivery

There are conflicting data on whether the day and time of birth has an independent effect on the risk of perinatal death

**WHAT THIS STUDY ADDS**

At term, the risk of neonatal death ascribed to anoxia was increased among women delivering outside the hours of the normal working week

About one in four deaths from intrapartum anoxia at term could be prevented if all women attempting vaginal birth had the same risk of this event as women delivering during the normal working week

events might be seen as out of proportion to the potential benefit. We analysed neonatal death from anoxia as a measurable end point. Although we were unable to study other consequences of intrapartum fetal anoxia, such as intrapartum stillbirth and severe non-lethal asphyxia leading to long term neurodevelopmental impairment, it is possible that these would be similarly related to delivery out of hours. Any interventions that improved outcomes out of hours would therefore be likely to have a greater effect than merely reducing the number of neonatal deaths. Furthermore, previous research has shown that interventions in early life provide better value in terms of the costs per years of life gained than interventions in later life.<sup>26</sup>

**Contributors:** DP, AMW, and GCSS formed the hypothesis and designed the study. MF did the linkage and extracted the data. DP, AMW, and GCSS performed the analysis and interpreted the results. DP and GCSS drafted the paper. All authors contributed to editing the draft for content and approved the final version of the paper. GCSS is guarantor.

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**Competing interest:** All authors have completed the unified competing interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare (1) no financial support for the submitted work from anyone other than their employer; (2) no financial relationships with commercial entities that might have an interest in the submitted work; (3) no spouses, partners, or children with relationships with commercial entities that might have an interest in the submitted work; and (4) no non-financial interests that may be relevant to the submitted work.

**Ethical approval:** This study was approved by the privacy advisory committee of the Information and Statistics Division of NHS Scotland. The chair of the Scotland A research ethics committee has stated that analysis of anonymised extracts of the linked data does not require separate ethical approval.

**Data sharing:** No additional data available.

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