

Rates of and Factors Associated With Delivery-Related Perinatal Death Among Term Infants in Scotland

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REPORTS FROM INDUSTRIALIZED countries have demonstrated decreases in the rates of perinatal mortality during the last 2 decades.¹⁻⁴ Much of the reduction in perinatal mortality is associated with advances in the management of infants delivered preterm.^{5,6} Mortality among US infants with a birth weight between 501 and 750 g decreased from approximately 60% in 1991 to less than 50% in 1997-2002.⁵ At term, after exclusion of antepartum stillbirth and perinatal death due to fetal abnormality, most intrapartum and neonatal deaths are associated with intrapartum anoxia.^{7,8} There are some data to suggest reduced rates of these deaths.^{1,9,10} However, interpretation of these data are complex, because no studies use data sets that combine detailed information on key obstetric characteristics, such as gestational age, presentation, and mode of delivery, and the key characteristics of the loss (cause and timing of the death).^{1,2,10}

A previous study in the United Kingdom used birth weight of more than 2500 g as a proxy for infants born at term and demonstrated reduced rates of intrapartum stillbirth but unchanged rates of neonatal death ascribed to intrapar-

Context Rates of obstetric intervention in labor, including cesarean delivery, have increased significantly in most developed countries. It is, however, unclear if this has been paralleled by decreased rates of perinatal and neonatal death associated with complications of labor at term.

Objectives To determine whether rates of perinatal death at term, either during labor or in the neonatal period, have changed in Scotland during the last 20 years and whether this was associated with a reduction in deaths ascribed to intrapartum anoxia.

Design, Setting, and Participants A population-based, retrospective cohort study of linked data from a registry of births (Scottish Morbidity Record 02) and a registry of perinatal deaths (Scottish Stillbirth and Infant Death Survey) between 1988 and 2007. Participants included all births of a singleton infant in a cephalic presentation at term (N=1 012 266), excluding those with perinatal death due to congenital anomaly or antepartum stillbirth.

Main Outcome Measure Delivery-related perinatal death, defined as intrapartum stillbirth or neonatal death unrelated to congenital abnormality. These events were also subdivided into those events ascribed to intrapartum anoxia and all other causes. The risk of death was modeled using logistic regression and analyses were adjusted for maternal age, height, parity, socioeconomic deprivation status, gestational age, birth weight percentile, fetal sex, onset of labor, and the annual number of births per hospital.

Results During the study period, the risk of delivery-related perinatal death decreased from 8.8 to 5.5 per 10 000 births (unadjusted change, -38%; 95% confidence interval [CI], -51% to -21%). When analyzed by the cause of death, there was a significant decrease in the risk of death ascribed to intrapartum anoxia (5.7 to 3.0 per 10 000 births; unadjusted change, -48%; 95% CI, -62% to -29%), but no significant change in the risk of death ascribed to other causes. When deaths ascribed to intrapartum anoxia were analyzed by the time of death in relation to delivery, the reduction was similar comparing intrapartum stillbirths (2.6 to 1.1 per 10 000 births; unadjusted change, -60%; 95% CI, -75% to -34%) and neonatal deaths (3.1 to 1.9 per 10 000 births; unadjusted change, -38%; 95% CI, -59% to -7%). Adjustment for maternal, fetal, and obstetric factors was without material effect.

Conclusion Rates of intrapartum stillbirth and neonatal death at term decreased in Scotland between 1988 and 2007. This decrease was only significant for deaths ascribed to intrapartum anoxia.

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tum anoxia.¹ A previous study of 3 hospitals in Dublin, Ireland, also demonstrated a decrease in intrapartum fetal death among singleton infants in a ce-

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phalic presentation at term from approximately 9 per 10 000 births in 1979 to 1 to 2 per 10 000 births in 2001-2003.¹⁰ However, this study lacked information on neonatal death. Neither study adjusted for variation in maternal characteristics such as age and parity.^{1,10}

We have previously used nationally collected data from Scotland to analyze risk factors for antepartum stillbirth and delivery-related perinatal death.^{8,11,12} However, our previous work did not address secular trends in these events. In this study, we used data from more than 1 million singleton births of an infant in a cephalic presentation at term during a 20-year period in Scotland and sought to determine (1) the trend of delivery-related perinatal death, (2) whether any decrease was associated with a reduction in the number of deaths ascribed to intrapartum anoxia, and (3) whether observed changes in rates of death were related to changes in associated maternal, infant, and obstetric factors.

METHODS

National Registers

The Scottish Morbidity Record 02 (SMR02) database collects information on clinical and demographic characteristics and outcomes of all patients discharged from Scottish maternity hospitals. The register is subjected to regular quality assurance checks and has been more than 99% complete since the late 1970s.¹³ A quality assurance exercise performed in 1996-1997 compared 5% of case records (n=1414) with the SMR02 database during a 6-month period. This exercise demonstrated that all fields used in our study had less than 2% errors, with the exception of maternal height (4.4%), estimated gestation (5.6%), and induction of labor (6.4%).¹¹

Records of singleton births from the SMR02 database between 1988 and 2007, inclusive, were linked to the Scottish Stillbirth and Infant Death Survey (SSBIDS), a national registry that routinely classifies all perinatal deaths in Scotland. Coding of the cause of death is performed by a single medically quali-

fied individual (the Scottish coordinator) in the Information and Statistics Division of the National Health Service 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 Registrar's Office, which is a legal requirement following perinatal death. The register is 100% complete when compared with the death certificate database and has been described in detail elsewhere.^{14,15} Approval for the record linkage was provided by the Privacy Advisory Committee of the Information and Statistics Division of the National Health Service Scotland.

Study Design and Participants

The study design is a population-based, retrospective cohort study composed of all singleton infants in a cephalic presentation delivered at term between 1988 and 2007. The exclusion criteria were multiple pregnancy, antepartum stillbirth, perinatal death ascribed to congenital abnormality or Rh isoimmunization, delivery outside 37 to 43 weeks' gestation, records with unknown mode of delivery, and deliveries in units with fewer than 10 deliveries per year.

Main Outcome Measures

There were 2 prespecified main outcomes: (1) delivery-related perinatal death and (2) a subgroup of these events in which the cause was ascribed to intrapartum anoxia. Delivery-related perinatal death was defined as intrapartum stillbirth or neonatal death at term, excluding deaths ascribed to congenital abnormality or Rh isoimmunization. Intrapartum stillbirth was defined as a stillbirth in which intrauterine fetal death occurred following the onset of labor but before birth. Neonatal death was defined as death during the first 4 weeks of life in a liveborn infant. Early neonatal death was defined as death of a liveborn infant between day 1 and day 7 (inclusive) of life where the day of birth is counted as day 1. Late neonatal death was defined as death of

a liveborn infant between days 8 and 28 (inclusive) of life. Both early and late neonatal deaths were included in the analysis, because deaths due to events in labor may occur beyond the early neonatal period.¹⁶

The cause of stillbirth and neonatal death was coded using a modification of the Wigglesworth classification.^{14,17} Deaths were classified according to direct obstetric causes (in order): congenital abnormality, isoimmunization, toxemia (preeclampsia/eclampsia), hemorrhage (antepartum), mechanical, maternal, miscellaneous, and unexplained. It is a hierarchical system which dictates that a perinatal death where there was severe preeclampsia complicated by abruption would be ascribed to toxemia because toxemia is above hemorrhage in the hierarchy. A death associated with a grossly abnormal fetal heart rate trace but without any of the above antecedents would be classified as unexplained obstetric cause. Intrauterine growth restriction is not regarded as an antecedent cause of death in the obstetric classification. Deaths were also classified according to pediatric causes (in order): congenital abnormality, isoimmunization, intrauterine anoxia (subdivided into antepartum or intrapartum), birth trauma, pulmonary complications of prematurity, intracranial hemorrhage, infection, hemorrhage (other than intracranial), miscellaneous, and unexplained (including sudden infant death syndrome). Death ascribed to congenital anomaly was defined as any structural or genetic defect incompatible with life or potentially treatable but causing death.¹⁷ Therefore, classification as death ascribed to intrapartum anoxia was on the basis of the pediatric classification and could be associated with a variety of obstetric antecedents. The definition of anoxia in this classification is broad and includes hypoxia, acidosis, and asphyxia.

We also performed an exploratory analysis to determine the plausibility of possible explanations of the trends observed. This included analysis of the trend in deaths ascribed to intrapartum anoxia in relation to (1) timing of

labor and (2) mode of delivery. We also explored changes in the rate of delivery of liveborn infants with a 5-minute Apgar score of less than 7 and analyzed the risk of neonatal death ascribed to intrapartum anoxia in this group. All analyses involving Apgar score were only performed on data between 1988 and 2003, inclusive, as information on Apgar score was less complete after 2003. This was due to systematic underreporting of Apgar score from the Tayside region of Scotland. Missing data on Apgar score were not imputed.

We adjusted analyses for maternal age, parity, height, socioeconomic deprivation, gestational age, fetal sex, birth weight percentile, induction of labor, and hospital throughput. All these characteristics except the following were defined as previously described.⁸ Hospital throughput was defined as the total number of births recorded in the SMR02 database for the given hospital over the given year. Assisted vaginal delivery was defined as vaginal delivery using either obstetric forceps or vacuum (ventouse). Emergency cesarean delivery was defined as any cesarean that was not scheduled in advance. It also included emergency procedures performed before the onset of labor and procedures performed due to arrested progress in labor in the absence of an urgent indication for delivery (such as fetal distress).

Statistical Analyses

Observed continuous variables were summarized by the median and interquartile range, and comparisons between groups were made by the Mann-Whitney *U* test. Univariate comparisons of dichotomous data were made by the χ^2 test. The risk of events was modeled by using logistic regression. Linearity of continuous variables in logistic regression models, including time, was tested by using fractional polynomials. Because missing covariates were likely to be missing at random and to avoid a loss in efficiency, missing data were imputed by using multiple imputation by chain equations.^{18,19} Five im-

putations were created using a set of appropriate imputation models constructed from all covariates and outcome variables in their raw scale. Missing values for maternal age, height, parity, socioeconomic deprivation status, fetal sex, birth weight, and onset of labor were imputed.

The modeled incidence of a given event in 1988 and 2007 was estimated from a univariate logistic regression model with year as a continuous variable, and these modeled values were used to illustrate the absolute change in incidence during the study period. Year was entered into the model as a scaled continuous variable in which 1988 equaled 0 and 2007 equaled 1. Therefore, the logistic regression model yielded an odds ratio (OR) for the given outcome during the 20-year period. This OR was then expressed as the percentage change over the study period, $[(OR-1) \times 100]$. Unadjusted and adjusted percentage changes were obtained by using the unadjusted and adjusted OR, respectively. Therefore, negative data indicated decreasing risk and positive data indicated increasing risk during the 20-year period. This was also performed for analysis of Apgar score, although this was confined to a 16-year period, to allow comparability of the proportional changes. Given that the primary outcome affected less than 0.1% of the population, odds and risk will be virtually identical; therefore, the terms are used interchangeably.

The Wald test was used to test the interaction between mode of delivery and the trend of delivery-related perinatal death during the study period. Clustered analysis at hospital and maternal level was performed to determine whether accounting for clustering of deliveries in maternity units and repeated deliveries to the same individual significantly altered the results. In the clustered logistic regression, univariate analysis was performed on both the whole population and the cases with no missing data. Multivariate analysis was only performed on those with complete data, due to the computational difficulty of performing logistic regres-

sion with both multiple imputation and clustered analysis in a data set of more than 1 million. *P* values for all the hypotheses were 2-sided and the statistical significance was set at $P < .05$. All analyses were performed by using Stata version 10.0 (StataCorp LP, College Station, Texas).

RESULTS

The linked SMR02 and SSBIDS databases contained 1 130 375 records of singleton births between 1988 and 2007. We excluded 68 646 records (6.1%) because gestation was less than 37 weeks, 294 records (0.03%) because gestation was more than 43 weeks, and 2403 records (0.2%) with missing data for gestation. Of the term deliveries, we excluded 775 perinatal deaths (0.1%) ascribed to congenital abnormality or Rh isoimmunization, 1659 antepartum stillbirths (0.2%), and 43 645 noncephalic deliveries (4.1%). Most of the noncephalic deliveries were cesarean deliveries (92.3%) and the most common presentation was breech ($n = 32\ 160$, 73.4%). We also excluded 283 records (0.03%) with unknown mode of delivery, 398 records (0.04%) because the deliveries were documented to have taken place in hospitals delivering fewer than 10 women per year, and 6 records (0.0005%) with inconsistent perinatal death classification. This resulted in a study cohort of 1 012 266 (some records had multiple exclusions), which corresponded to 95.6% of all singleton term births in Scotland between 1988 and 2007.

There were 719 delivery-related perinatal deaths (0.07%) during the study period. This consisted of 219 intrapartum stillbirths (30.5%) and 500 neonatal deaths (69.5%). The autopsy rate was 66.2% ($n = 476$) and did not significantly vary during the study period ($P = .35$). Of the 719 delivery-related perinatal deaths, 432 (60.1%) were ascribed to intrapartum anoxia and 287 (39.9%) were ascribed to other causes (TABLE 1). In 141 (32.6%) of the deaths ascribed to intrapartum anoxia, there was a coexisting obstetric event (eg, cord prolapse, severe pre-

eclampsia, or placental abruption). Neonatal deaths ascribed to intrapartum anoxia occurred earlier than those ascribed to other causes (FIGURE 1).

The characteristics of the cohort are tabulated by outcome (TABLE 2). Women with deliveries resulting in death ascribed to intrapartum anoxia were shorter, more likely to be primiparous, deliver in smaller obstetric units, and were less likely to live in areas of either very high or very low socioeconomic status. Women with deliveries resulting in deaths ascribed to causes other than intrapartum anoxia were younger and more likely to have labor induced. Women with either adverse outcome were more likely to be delivered by emergency cesarean and their infants tended to be smaller. Perinatal death ascribed to intrapartum anoxia was positively associated with a longer duration of labor and assisted vaginal delivery. There were no deaths ascribed to intrapartum anoxia among women delivered by planned cesarean.

The absolute risk of delivery-related perinatal death in the population was 7.1 per 10 000 births (95% confidence interval [CI], 6.6-7.6). The incidence of perinatal death ascribed to intrapartum anoxia (4.3 per 10 000 births; 95% CI, 3.9-4.7) was higher than the incidence of perinatal death ascribed to other causes (2.8 per 10 000 births; 95% CI, 2.5-3.2). When modeled between 1988 and 2007 (TABLE 3), there was a decrease in the risk of delivery-related perinatal death from 8.8 to 5.5 per 10 000 births (unadjusted percentage change, -38%; 95% CI, -51% to -21%). When analyzed by the cause of death, there was a statistically significant decrease in the incidence of death ascribed to intrapartum anoxia from 5.7 to 3.0 per 10 000 births (unadjusted percentage change, -48%; 95% CI, -62% to -29%), but no statistically significant decrease in the incidence of deaths ascribed to other causes (3.1 to 2.5 per 10 000 births; unadjusted percentage change, -19%; 95% CI, -45% to 19%) (FIGURE 2). Fractional polynomials demonstrated no improvement in the fit of the line model-

Table 1. Obstetric Classification of Causes of Intrapartum Stillbirth and Neonatal Death^a

Obstetric Classification	Pediatric Classification	
	Intrapartum Anoxia (n = 432)	Other Causes (n = 287) ^b
Intrapartum stillbirth (n = 219)		
Toxemia, preeclampsia/eclampsia	6	0
Hemorrhage, antepartum	41	5
Mechanical	20	3
Maternal disorder, including infection	3	13
Miscellaneous	0	3
Unexplained	111	14
Neonatal death (n = 500)		
Preeclampsia	6	3
Hemorrhage	23	6
Mechanical	34	7
Maternal disorder, including infection	3	33
Miscellaneous	5	17
Unexplained	180	183

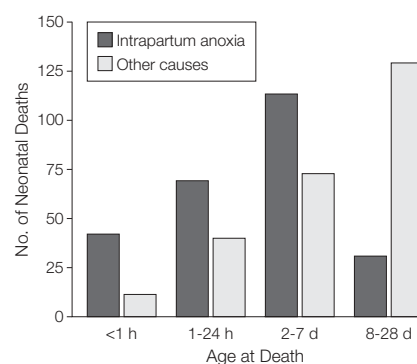
^aThe cause of intrapartum stillbirth and neonatal death was coded using a modification of the Wigglesworth classification.¹⁴ The proportions of autopsies were anoxic intrapartum stillbirth (60.8%), nonanoxic intrapartum stillbirth (81.6%), anoxic neonatal death (61.8%), and nonanoxic neonatal death (72.3%) ($P = .01$).

^bThe pediatric classifications in this category were antepartum anoxia (n=40); birth trauma (n=6); pulmonary complications of prematurity (n=3); intracranial hemorrhage (n=5); infection (n=88); hemorrhage, other (n=10); miscellaneous (n=30); and unexplained, including sudden infant death syndrome (n=105).

ing the decrease in risk during the study period for delivery-related perinatal death compared with a linear term for either all-cause mortality ($P = .73$) or deaths ascribed to intrapartum anoxia ($P > .99$). The magnitude of the decrease in the incidence of deaths ascribed to intrapartum anoxia was comparable between intrapartum stillbirth (2.6 to 1.1 per 10 000 births; unadjusted percentage change, -60%; 95% CI, -75% to -34%) and neonatal death (3.1 to 1.9 per 10 000 births; unadjusted percentage change, -38%; 95% CI, -59% to -7%). Adjustment for maternal, fetal, or obstetric characteristics did not reduce the magnitude of decrease in the risk of delivery-related perinatal death or in the subgroup ascribed to intrapartum anoxia (Table 3).

When the analysis was confined to women in labor, the incidence of perinatal death ascribed to intrapartum anoxia more than halved during the study period (5.2 to 2.4 per 10 000 births; unadjusted percentage change, -55%; 95% CI, -69% to -35%). When stratified by mode of delivery, the magnitude of change in the risk of perinatal death ascribed to intrapartum anoxia was similar comparing those newborns delivered vaginally (spontaneous vaginal

Figure 1. Timing of Neonatal Deaths Ascribed to Intrapartum Anoxia and Other Causes



Pediatric classifications in the other causes category included antepartum anoxia, birth trauma, pulmonary complications of prematurity, intracranial hemorrhage, infection, hemorrhage (other), miscellaneous, and unexplained (including sudden infant death syndrome). Comparing deaths ascribed to intrapartum anoxia with deaths ascribed to other causes, $P < .001$ by χ^2 test.

delivery: 2.9 to 1.5 per 10 000 births; unadjusted percentage change, -48%; 95% CI, -69% to -12%; and assisted vaginal delivery: 12.4 to 3.7 per 10 000 births; unadjusted percentage change, -71%; 95% CI, -85% to -41%) with those delivered by emergency cesarean (26.2 to 6.4 per 10 000 births; unadjusted percentage change, -75%; 95% CI, -88% to -50%). There was no evi-

dence that the magnitude of the decrease differed in relation to mode of delivery in either the unadjusted (*P* for interaction = .49) or adjusted models (*P* for interaction = .16).

The incidence of liveborn infants delivered following labor with a 5-minute Apgar score of less than 7 in the study population between 1988 and 2003 was 13.4 per 1000 livebirths (95% CI, 13.2-13.7; n = 10 366). The risk of neonatal

death in these infants was 16.3 per 1000 births (95% CI, 14.0-18.9), which was much greater than the risk of death in infants with 5-minute Apgar score of 7 or more (OR, 70.3; 95% CI, 57.0-86.8). Most (82.3%) of the neonatal deaths in this group were ascribed to intrapartum anoxia. Between 1988 and 2003, the incidence of infants delivered following labor with a 5-minute Apgar score of less than 7 decreased

from 16.9 to 10.2 per 1000 births (unadjusted percentage change expressed for a 20-year period, -48%; 95% CI, -52% to -43%) (FIGURE 3). When the analysis was confined to this group, there was no statistically significant decrease in the incidence of neonatal death ascribed to intrapartum anoxia (14.2 to 12.4 per 1000 births; unadjusted percentage change expressed for a 20-year period, -16%; 95% CI, -59% to

Table 2. Characteristics of Cohort by Categories of Perinatal Outcome

Characteristics	Survived (n = 1 011 547)	Delivery-Related Perinatal Death (n = 719)			
		Intrapartum Anoxia (n = 432)	<i>P</i> Value ^a	Other Causes (n = 287)	<i>P</i> Value ^a
Maternal					
Age, median (IQR), y ^b	28 (24-32)	28 (24-32)	.10	26 (22-31)	<.001
Height, median (IQR), cm	163 (158-167)	162 (157-165)	.01	162 (157-166)	.19
Missing value, No. (%)	157 942 (15.6)	71 (16.4)	.64	57 (19.9)	.05
Parity, No. (%) ^b					
0	450 959 (44.6)	243 (56.3)	<.001	145 (50.5)	.07
1-2	494 909 (49.0)	163 (37.7)		123 (42.9)	
>2	64 780 (6.4)	26 (6.0)		19 (6.6)	
Deprivation category, No. (%)					
1 (Least deprived)	55 271 (5.5)	14 (3.2)	.04	19 (6.6)	.40
2	137 562 (13.6)	60 (13.9)		32 (11.2)	
3	209 222 (20.7)	83 (19.2)		50 (17.4)	
4	251 176 (24.8)	121 (28.0)		84 (29.3)	
5	157 772 (15.6)	69 (16.0)		44 (15.3)	
6	118 434 (11.7)	62 (14.4)		34 (11.9)	
7 (Most deprived)	76 618 (7.6)	21 (4.9)	.82	24 (8.4)	.20
Missing value	5492 (0.5)	2 (0.5)		0	
Infant					
Gestational age, median (IQR), wk	40 (39-41)	40 (39-41)	.22	40 (38-40)	<.001
Male sex, No. (%) ^b	517 742 (51.2)	230 (53.2)	.39	141 (49.1)	.49
Birth weight, median (IQR), g ^b	3450 (3130-3780)	3400 (3020-3790)	.046	3180 (2900-3580)	<.001
Obstetric					
Onset of labor, No. (%) ^b					
Spontaneous onset	756 457 (74.9)	317 (73.4)	.53	204 (71.3)	.17
Augmentation of labor	100 905 (10.0)	36 (8.4)	.26	27 (9.4)	.76
Prostaglandin induction	152 892 (15.1)	78 (18.1)	.09	55 (19.2)	.05
Duration of labor, median (IQR), h ^c	6 (4-10)	8 (4-12)	<.001	6 (4-10)	.19
Mode of delivery, No. (%)					
Spontaneous vaginal	738 907 (73.1)	163 (37.7)	<.001	178 (62.0)	<.001
Assisted vaginal	129 217 (12.8)	96 (22.2)	<.001	35 (12.2)	.77
Planned cesarean	48 301 (4.8)	0	<.001	9 (3.1)	.19
Emergency cesarean	95 122 (9.4)	173 (40.1)	<.001	65 (22.7)	<.001
Hospital throughput, deliveries per year, No. (%)					
<1000	73 501 (7.3)	34 (7.9)	.02	22 (7.7)	.90
1000-1999	180 142 (17.8)	103 (23.8)		45 (15.7)	
2000-2999	208 802 (20.6)	82 (19.0)		58 (20.2)	
3000-3999	251 704 (24.9)	104 (24.1)		74 (25.8)	
≥4000	297 398 (29.4)	109 (25.2)		88 (30.7)	

Abbreviation: IQR, interquartile range.

^aMann-Whitney *U* and χ^2 tests were used as appropriate and compared with live births.

^bSmall number of missing values in other variables for maternal age, 291 (0.03%); parity, 899 (0.09%); sex, 26 (0.003%); birth weight, 297 (0.03%); and onset of labor, 1295 (0.13%).

^cSummary statistics confined to women in labor.

72%). Adjustment of these associations for maternal, obstetric, and fetal factors was without material effect (adjusted OR, 0.69; 95% CI, 0.32-1.47; adjusted percentage change, -31%; 95% CI, -68% to 47%).

During the study period, the rate of cesarean delivery approximately doubled in the full cohort (from 8.9% to 21.6%, $P < .001$). This was associated with an increase in both the rate of planned cesarean delivery (from 2.7%

to 7.8%, $P < .001$) and emergency cesarean delivery among women in active labor (from 4.7% to 10.4%, $P < .001$). There was a significant negative relationship between the annual cesarean delivery rate and the annual rate of delivery-related perinatal death ascribed to intrapartum anoxia, but not to other causes (FIGURE 4).

The decrease observed in perinatal death ascribed to intrapartum anoxia in the whole study population was not

affected by analytic methods that corrected standard errors for clustering at maternal (unadjusted percentage change, -48%; 95% CI, -62% to -29%) and hospital level (unadjusted percentage change, -48%; 95% CI, -61% to -32%). In the complete case analysis, the unadjusted and adjusted percentage change in the incidence of perinatal death ascribed to intrapartum anoxia was not affected by clustered analysis at maternal level (unadjusted,

Table 3. Trend of Perinatal and Neonatal Death During the Study Period by Cause and Timing of Death^a

Delivery-Related Perinatal Death	Change in the Incidence of Delivery-Related Perinatal Death Between 1988 and 2007					
	Unadjusted			Adjusted ^b		
	OR (95% CI)	% Change (95% CI)	P Value ^c	OR (95% CI)	% Change (95% CI)	P Value ^c
All-cause (n = 719) ^d	0.62 (0.49 to 0.79)	-38 (-51 to -21)	<.001	0.57 (0.44 to 0.74)	-43 (-56 to -26)	<.001
Intrapartum anoxia (n = 432)	0.52 (0.38 to 0.71)	-48 (-62 to -29)	<.001	0.46 (0.33 to 0.65)	-54 (-67 to -35)	<.001
Intrapartum stillbirth (n = 181)	0.40 (0.25 to 0.66)	-60 (-75 to -34)	<.001	0.42 (0.25 to 0.70)	-58 (-75 to -30)	.001
Neonatal death (n = 251)	0.62 (0.41 to 0.93)	-38 (-59 to -7)	.02	0.50 (0.32 to 0.77)	-50 (-68 to -23)	.002
Other causes (n = 287)	0.81 (0.55 to 1.19)	-19 (-45 to 19)	.28	0.76 (0.51 to 1.14)	-24 (-49 to 14)	.19

Abbreviations: CI, confidence interval; OR, odds ratio.

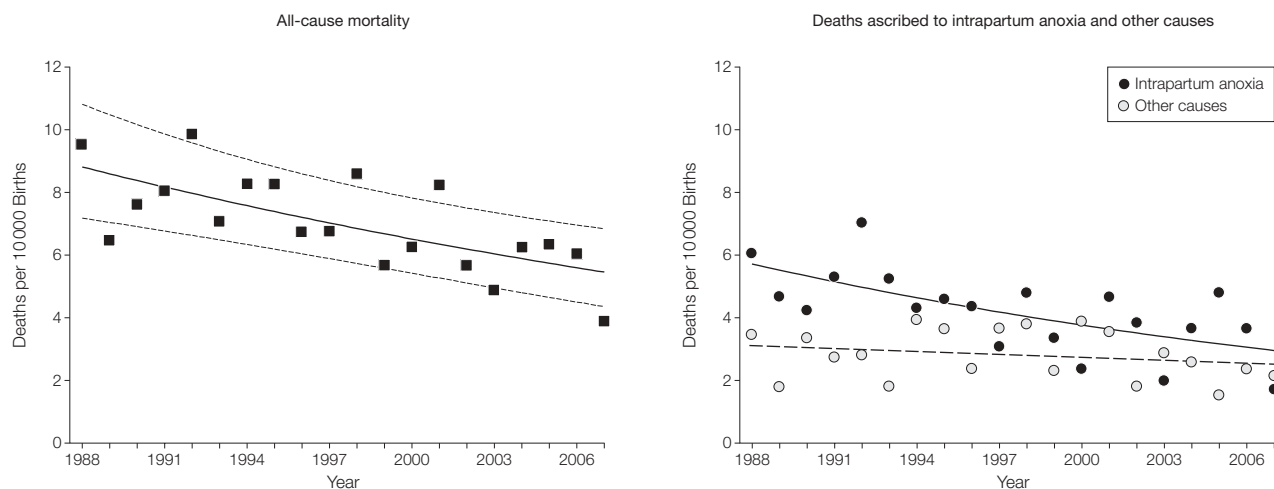
^aUnadjusted and adjusted ORs are also expressed as the percentage change over the study period $[(OR-1) \times 100]$, using the unadjusted or adjusted ORs, as appropriate. Negative data indicate a decreasing risk, and positive data indicate an increasing risk during the 20-year period.

^bAdjusted for maternal age, height, parity, socioeconomic deprivation status, gestational age, birth weight percentile, fetal sex, onset of labor, and hospital throughput.

^cTest of significance of change in the rate of perinatal death obtained from the logistic regression model.

^dThe other factors that were statistically significantly associated with all-cause delivery-related perinatal death in multivariate analysis were maternal age of at least 40 years (unadjusted OR, 1.90; 95% CI, 1.24-2.89; adjusted OR, 2.12; 95% CI, 1.38-3.26); primiparous (unadjusted OR, 1.49; 95% CI, 1.28-1.73; adjusted OR, 1.46; 95% CI, 1.24-1.72); birth weight of 10th percentile or less (unadjusted OR, 2.18; 95% CI, 1.78-2.67; adjusted OR, 2.03; 95% CI, 1.65-2.49); and birth weight of at least 98th percentile (unadjusted OR, 2.11; 95% CI, 1.44-3.08; adjusted OR, 2.30; 95% CI, 1.56-3.40).

Figure 2. Incidence and Trend of Delivery-Related Perinatal Death Ascribed to All-Cause Mortality and Intrapartum Anoxia and Other Causes in Scotland Between 1988 and 2007



For all-cause mortality, the solid fitted line is the predicted probability from a univariate logistic regression model with year as a linear predictor; dashed curves are the associated 95% confidence intervals (unadjusted odds ratio [OR], 0.62; 95% CI, 0.49-0.79). For deaths ascribed to intrapartum anoxia and other causes, the solid fitted line is the modeled value for death ascribed to anoxia and the dashed fitted line is the modeled value for deaths ascribed to other causes, with the associated 95% CIs omitted for clarity (intrapartum anoxia: unadjusted OR, 0.52; 95% CI, 0.38-0.71; other causes: unadjusted OR, 0.81; 95% CI, 0.55-1.19). Pediatric classifications in the other causes category included antepartum anoxia, birth trauma, pulmonary complications of prematurity, intracranial hemorrhage, infection, hemorrhage (other), miscellaneous, and unexplained (including sudden infant death syndrome).

-47%; 95% CI, -63% to -25%; adjusted, -50%; 95% CI, -65% to -27%) or hospital level (unadjusted, -47%; 95% CI, -62% to -26%; adjusted, -50%; 95% CI, -64% to -30%).

COMMENT

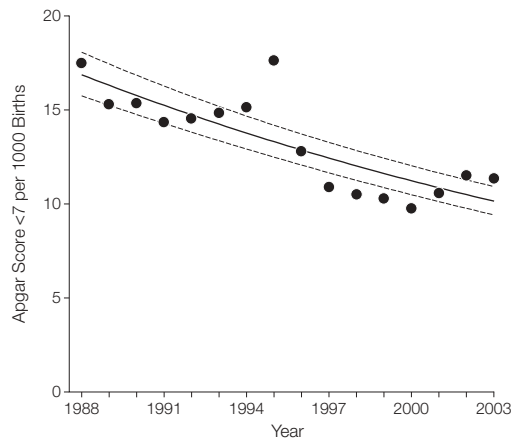
The key finding of our analysis is that rates of death ascribed to intrapartum anoxia in term infants declined in Scotland between 1988 and 2007. This can-

not be explained by increased rates of planned cesarean delivery for breech presentation^{20,21} because the analysis was confined to infants in a cephalic presentation. The decrease was observed across all modes of delivery. Adjustment for changes in maternal age, height, parity, socioeconomic deprivation status, gestational age, fetal sex, birth weight percentile, onset of labor, and hospital throughput was without

material effect. The rate of decrease was similar comparing deaths during labor (intrapartum stillbirth) and deaths in the neonatal period. The decrease was only significant for perinatal deaths ascribed to intrapartum anoxia.

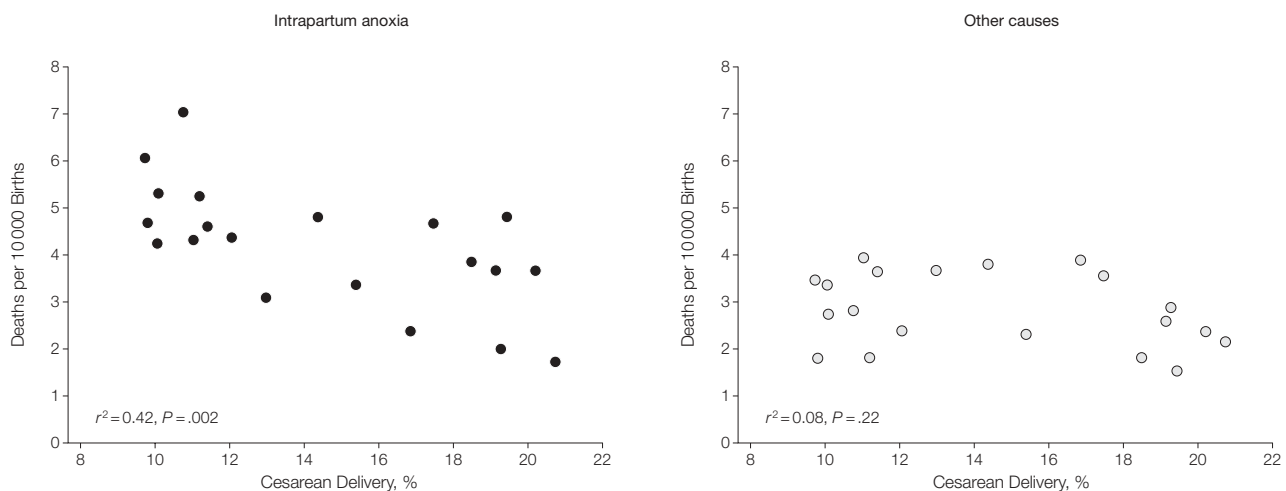
Broadly speaking, there are 2 potential explanations for reduced rates of perinatal death ascribed to intrapartum anoxia at term, namely, reduced rates of fetuses experiencing severe anoxia during labor or improved resuscitation of anoxic infants who were liveborn. Our interpretation of our analysis is that the observed changes are most likely to reflect reduced rates of fetuses experiencing severe anoxia during labor. First, there were similar proportional reductions in the rates of intrapartum stillbirth and neonatal death. Improved neonatal resuscitation cannot result in reduced rates of intrauterine death. Second, there was a decrease in the total number of infants born with a depressed Apgar score (ie, including both neonatal death and survivors). Third, when the analysis was confined to liveborn infants delivered with a depressed 5-minute Apgar score, there was no statistically significant decrease in the risk of neonatal death. The analyses using the Apgar score should,

Figure 3. Incidence and Trend of 5-Minute Apgar Score of Less Than 7 per 1000 Births in Scotland Between 1988 and 2003



The solid fitted line is the predicted probability from a univariate logistic regression model with year as a linear predictor; dashed curves are the associated 95% confidence intervals (unadjusted odds ratio, 0.52; 95% confidence interval, 0.48-0.57).

Figure 4. Annual Rate of Delivery-Related Perinatal Death Ascribed to Intrapartum Anoxia and Other Causes vs Cesarean Delivery Rate



Each point represents the pair of values for a given year. The period of analysis was between 1988 and 2007. Pediatric classifications in the other causes category included antepartum anoxia, birth trauma, pulmonary complications of prematurity, intracranial hemorrhage, infection, hemorrhage (other), miscellaneous, and unexplained (including sudden infant death syndrome).

however, be interpreted cautiously because the Apgar score is not a particularly good measure of anoxia, these were secondary analyses, and the CIs of the estimated reduction in the risk of death among the group with a depressed Apgar score were wide.

Secondary analyses of routinely collected data must be interpreted cautiously because data quality will generally be less detailed and reliable than in prospective studies.²² Furthermore, classification of the cause of perinatal death can be complex and multiple different systems have been described.²³ However, the decrease in the number of deaths ascribed to anoxia is unlikely to be due to misclassification of the cause of death. In the data source used, classification of the cause of death was performed by a medically qualified individual (the Scottish coordinator of the SSBIDS) with autopsy information available. Approximately two-thirds of the infants had an autopsy performed and the proportion did not change during the study period. This proportion is higher than previously reported in other parts of the United Kingdom.²⁴ Previous studies have indicated that autopsy altered the diagnosis in up to 20% of cases,²⁴ although it is plausible that the proportion may be lower in cases ascribed to anoxia due to the availability of other diagnostic methods (such as cord blood pH, cardiotocography, and clinical assessment of the neonate). This latter point may explain the slightly lower autopsy rate among infants in which death was ascribed to anoxia. However, the rate of autopsy in cases in which death was ascribed to anoxia was still more than 60%. Even assuming that 20% of the diagnoses would have been changed had an autopsy been performed in the remaining 40%, this would only have changed the diagnosis in approximately 8% of all cases ascribed to intrapartum anoxia. Therefore, it is unlikely that bias due to misclassification of the cause of death could have significantly affected the findings.

We lacked the further detailed information required to determine why the

number of fetuses experiencing severe anoxia during labor may have decreased during the study period. The association was not materially affected by statistical adjustment for maternal age, height, parity, socioeconomic deprivation status, gestational age, birth weight percentile, fetal sex, onset of labor, and hospital throughput. However, we lacked information on other maternal characteristics that could plausibly have changed during the study period and could affect the risk of complications, such as maternal body mass index. We also lacked important clinical data that might help explain variation in rates of intrapartum anoxia, such as use of electronic fetal monitoring, regional anesthesia, and fetal blood sampling. Although randomized controlled trials of routine electronic fetal monitoring have failed to demonstrate reduction in the risk of perinatal death, the meta-analysis of these trials is underpowered to detect an effect.²⁵ Furthermore, many different aspects of obstetric care could contribute to changes in perinatal mortality, including general improvements in manpower, training, teamwork, and multidisciplinary working. The reduced rate of deaths ascribed to anoxia could also reflect a general improvement in the health of the population leading, for example, to reduced rates of events leading to anoxia (eg, abruptio).

The decrease in delivery-related perinatal deaths ascribed to anoxia coincided with a marked increase in rates of cesarean delivery, and more liberal use of this procedure is another potential explanation of the finding. We plotted the annual rate of delivery-related perinatal death against the annual cesarean delivery rate and observed a negative relationship for delivery-related perinatal deaths ascribed to anoxia, but not to other causes (Figure 4). The apparent relationship between these 2 rates must be interpreted with caution. The relationship could be explained by variation in other risk factors for each outcome or by changes in the characteristics of the population during the 20-year period. An influen-

tial World Health Organization study²⁶ had previously compared the perinatal mortality rate of countries in relation to their national rates of cesarean delivery. The interpretation of the analysis was that increasing the cesarean delivery rate above 10% to 15% was unlikely to be associated with improvement in perinatal mortality. However, total perinatal mortality includes causes of death that are largely independent of mode of delivery, such as antepartum stillbirth, neonatal death associated with prematurity, and deaths due to congenital abnormality. Moreover, variation in the cesarean delivery rate between countries has multiple possible explanations. Our analysis has the advantages that we studied cesarean delivery rates in a relatively homogeneous population with free access to health care and related this to perinatal deaths that were ascribed to complications of labor and delivery. However, both observations should be interpreted with caution due to multiple other unmeasured factors. Nevertheless, the current finding of a negative association between perinatal mortality rates and cesarean delivery rates of more than 15% suggests that this threshold may no longer be appropriate.

A number of previous studies^{1,2,9,10,27-30} from developed countries have demonstrated a decrease in the incidence of perinatal mortality. Most of these articles have not distinguished perinatal mortality by the timing of death in relation to labor, the cause of perinatal death, or both.^{2,9,27-30} Therefore, it is difficult to infer the basis for the observed reduction in these analyses. Studies that reported trends of perinatal mortality by the cause of death have found a decrease in the incidence of death due to intrapartum anoxia.^{1,9,27} However, several of these analyses included preterm births.^{2,9,27} It is recognized that, after exclusion of antepartum stillbirths, prematurity is the most common cause of neonatal death. In recent years, improvements in neonatal resuscitation and intensive care have significantly improved survival of infants born preterm.^{5,6} Given the pro-

found changes that have taken place in neonatal care, it is difficult to determine the relative contribution of changes in obstetric and neonatal care from studies that include preterm births. A study¹⁰ from Ireland in 2008 examined the incidence of intrapartum stillbirth confined to singleton infants in a cephalic presentation born at term. The authors described an absolute risk of this event of 3 per 10 000 births,¹⁰ which is similar to that observed in our study. These authors also found that the rates of intrapartum stillbirth decreased and that this was associated with a reduction in deaths ascribed to anoxia. However, this study only analyzed intrapartum deaths because they lacked data on neonatal death. Changes in obstetric care could result in a shift in the timing of perinatal death in relation to birth. A reduction in intrapartum stillbirth may be associated with an increased incidence of delivery of very severely anoxic live-born infants; therefore, any reduction in intrapartum death could be balanced by

increased rates of neonatal death. We were able to address this directly and observed comparable decreases in intrapartum and neonatal losses.

In conclusion, our findings demonstrate a 38% decrease in the incidence of intrapartum stillbirth and neonatal death in Scotland between 1988 and 2007 among singleton births at term with cephalic presentation. This was associated with a reduction in the number of deaths ascribed to intrapartum anoxia. The magnitude of the decrease in incidence was not affected by adjustment for measured changes in maternal, fetal, and obstetric characteristics. The pattern of the decline suggests that this was primarily due to a reduced number of severely anoxic infants rather than improved neonatal resuscitation. The change was paralleled by increased rates of cesarean delivery, but there is no direct evidence supporting a causal association between the 2 trends.

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Health and Primary Care (Dr Wood), University of Cambridge, Cambridge, England; Public Health Section, University of Glasgow, Glasgow, Scotland (Dr Pell); Information and Statistics Division, National Health Service National Services Scotland, Paisley, Scotland (Mr Fleming); and National Institute for Health Research Cambridge Comprehensive Biomedical Research Center, Cambridge, England (Dr Smith).

Author Contributions: Drs Pasupathy and Smith had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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