

ORIGINAL ARTICLE

Previous Preterm and Small-for-Gestational-Age Births and the Subsequent Risk of Stillbirth

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ABSTRACT

BACKGROUND

Some causes of stillbirth may also lead to fetuses that are small for gestational age (have a low birth weight with respect to their gestational age) or are delivered preterm (before 37 weeks of gestation). It is not known whether the birth of a previous small-for-gestational-age or preterm infant increases the subsequent risk of stillbirth.

METHODS

We assessed the associations between previous adverse outcomes of pregnancy and the risk of stillbirth in a nationwide Swedish study of 410,021 women who delivered first and second consecutive singleton infants between 1983 and 1997. There were 1842 and 1062 stillbirths during the first and second pregnancies, respectively.

RESULTS

As compared with women whose first infant was born at term (37 weeks of gestation or more) and was not small for gestational age, women whose first infant was born at term or preterm and was small for gestational age had an increased risk of stillbirth during their second pregnancy. The odds ratios for subsequent stillbirth, after adjustment for covariates known to be associated with an increased risk of stillbirth, were 2.1 (95 percent confidence interval, 1.6 to 2.8) among women with a first infant who was born at term and was small for gestational age, 3.4 (95 percent confidence interval, 2.1 to 5.6) among women with a first infant who was moderately (32 to 36 weeks of gestation) preterm and small for gestational age, and 5.0 (95 percent confidence interval, 2.5 to 9.8) among women with a first infant who was very (before 32 weeks of gestation) preterm and was small for gestational age. The odds ratio for subsequent stillbirth among women with a first stillborn infant was 2.5 (95 percent confidence interval, 1.4 to 4.7), as compared with women whose first infant was not stillborn. The rates of stillbirth in second pregnancies ranged from 2.4 per 1000 births among women whose first infant was born at term and was not small for gestational age to 19.0 per 1000 births among women whose first child was very preterm and was small for gestational age.

CONCLUSIONS

Delivery of a previous small-for-gestational-age infant is an important predictor of the subsequent risk of stillbirth, particularly if the infant was delivered preterm.

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STILLBIRTH ACCOUNTS FOR MORE THAN half of perinatal deaths in developed nations,¹ and the rates of stillbirth range from 3 to 4 per 1000 births in Sweden and the United States.^{2,3} Although the cause of stillbirths is poorly understood, fetal growth restriction may be one of the major determinants. Fetuses that are small for gestational age, commonly defined as a birth weight for gestational age that is below the 10th percentile or more than 2 SD below the mean, have an increased risk of stillbirth,⁴ especially preterm stillbirth.⁵ Congenital malformations, placental abruption, and intrauterine infections are also associated with an increased risk of stillbirth,⁶⁻⁹ and they may also increase the risk of other adverse outcomes, including preterm birth and the delivery of an infant who is small for gestational age.¹⁰⁻¹³

The tendency for adverse pregnancy outcomes to be repeated in successive births is well known, and the risk of stillbirth is estimated to increase by a factor of 2 to 10 among women with a prior stillbirth.^{14,15} A history of stillbirth also increases the likelihood of having a subsequent infant who is small for gestational age¹⁶ or has a reduced birth weight.¹⁷ Moreover, among women whose first pregnancy ended in stillbirth, the risk of having a small-for-gestational-age infant in a subsequent pregnancy is higher among those in whom the stillbirth was assessed clinically to be related to growth restriction than among those with a previous stillbirth that was not related to growth restriction.¹⁸ Women whose first pregnancy was complicated by a stillbirth with an unknown cause have an increased risk of preterm delivery during their second pregnancy.¹⁷

However, little is known about the influence of previous delivery of a small-for-gestational-age infant or preterm birth on the risk of stillbirth in a subsequent pregnancy. Using the nationwide Swedish Medical Birth Register, we studied more than 400,000 women who had two successive singleton births between 1983 and 1997 in order to determine previous adverse pregnancy outcomes, including stillbirth and the delivery of a small-for-gestational-age or preterm infant, and their associations with the risk of stillbirth in subsequent pregnancies. Since the likelihood of fetal growth restriction may be higher in premature infants who are small for gestational age,^{19,20} we also studied the joint effect of gestational age and birth weight for gestational age in the first pregnancy on the subsequent risk of stillbirth.

METHODS

STUDY DESIGN

The Birth Register, which includes information on more than 99 percent of births in Sweden, recorded more than 1.5 million singleton births between January 1, 1983, and December 31, 1997. Our study population was restricted to 410,021 women who delivered first and second consecutive singleton infants. The Birth Register includes demographic data and prospectively collected information on reproductive history and complications that occur during pregnancy, delivery, and the neonatal period. By means of each individual's unique national registration number, the Birth Register can be linked with other Swedish data sources.

In Sweden, maternal characteristics are recorded in a standardized manner during a woman's first visit for antenatal care, which occurs before the 15th week of gestation in more than 95 percent of the pregnancies.²¹ We used information on maternal characteristics from each woman's second pregnancy. Women were categorized as nonsmokers, moderate smokers (1 to 9 cigarettes per day), or heavy smokers (at least 10 cigarettes per day). The family situation was defined according to whether or not the woman was living with the baby's father. Maternal age was categorized as less than 25 years, 25 to 29 years, 30 to 34 years, or 35 years or older. Height measurements during the second pregnancy were categorized as 159 cm or less, 160 to 164 cm, 165 to 169 cm, or 170 cm or more. From height and weight measurements we calculated the body-mass index (the weight in kilograms divided by the square of the height in meters). Women were categorized according to the body-mass index as lean (a body-mass index of less than 20.0), normal (a body-mass index of 20.0 through 24.9), overweight (a body-mass index of 25.0 through 29.9), or obese (a body-mass index of 30.0 or more). Height and weight measurements were available only from 1992 onward. The year of the second delivery was divided into three groups: 1983 through 1989, 1990 through 1993, and 1994 through 1997. The interpregnancy interval was calculated as the number of months between the birth of the first child and the estimated date of conception of the second child and categorized as 0 to 3 months, 4 to 7 months, 8 to 11 months, 12 to 35 months, 36 to 71 months, or 72 months or more. Through linkage with the Education Register, information on the number of years of formal education completed as of December 31,

1998, was obtained and categorized as 11 or fewer years or 12 or more years. Information on the mother's country of birth was obtained through linkage to the Immigration Register and classified as Nordic (Sweden, Denmark, Norway, Finland, and Iceland) or non-Nordic. Maternal disorders were classified according to the 8th, 9th, and 10th revisions of the *International Classification of Diseases* (ICD-8, ICD-9, and ICD-10, respectively), and were noted at the time of the woman's discharge from the hospital. Hypertensive disease was defined as chronic hypertension, gestational hypertension, preeclampsia, and eclampsia (ICD-8 codes 637.0, 637.1, and 637.9; ICD-9 code 642; and ICD-10 codes O10, O11, O13, O14, O15, and O16). Antepartum hemorrhage was defined as placental abruption, placenta previa, and other reasons for antepartum bleeding (ICD-8 codes 632 and 651, ICD-9 code 641, and ICD-10 codes O44, O45, and O46).

A woman's first delivery was categorized as a livebirth or a stillbirth. There were 1842 stillbirths during the first pregnancy. We defined very preterm birth as live birth before 32 completed weeks of gestation, moderately preterm birth as live birth at 32 to 36 completed weeks of gestation (from 32 weeks 0 days through 36 weeks 6 days), and term birth as live birth at 37 or more completed weeks of gestation. Small-for-gestational-age birth was defined as one with a birth weight that was more than 2 SD below the mean for gestational age on the Swedish reference curve of estimated fetal growth.²² Live births were subclassified into six categories: not-small-for-gestational-age term, moderately preterm, and very preterm births and small-for-gestational-age term, moderately preterm, and very preterm births. In the Swedish Birth Register, stillbirth is defined as fetal death at 28 weeks of gestation or later; there is no information about the underlying cause of death. To determine gestational age, we used the results of ultrasonography performed early in the second trimester, a procedure that has been offered to all pregnant women in Sweden since 1990, 95 percent of whom accept it.²³ When this information was not available, gestational age was estimated from the date of a woman's last menstrual period.

The study was approved by the research ethics committee at Karolinska Institutet, Stockholm, Sweden. The research ethics committee did not require the women to provide informed consent.

STATISTICAL ANALYSIS

We used unconditional logistic-regression analysis to model the risk that the second birth would be a stillbirth as a function of the reproductive outcome of the first birth and maternal characteristics. Term liveborn infants who were not small for gestational age were used as the reference category. Odds ratios were calculated before and after adjustment for maternal characteristics and pregnancy complications.

In further analyses, we investigated the risks of preterm and term stillbirth during the second birth and of having a small-for-gestational-age stillborn infant or a stillborn infant who was not small for gestational age during the second birth. Adjusted odds ratios were estimated to model the risk of these specific subtypes of stillbirth in the second birth as a function of the reproductive outcome of the first birth.

RESULTS

The overall rate of stillbirth during the second pregnancy was 2.6 per 1000 births (total, 1062), and the rates of stillbirth ranged from 2.4 per 1000 among women whose first child was born at term and was

Table 1. Outcomes of the First Pregnancy and Univariate Associations with the Risk of Stillbirth during the Second Pregnancy among Women Who Had Two Successive Singleton Births in Sweden between 1983 and 1997.

Outcome of First Pregnancy	Second Births		
	Total No.	No. of Stillbirths (Rate/1000 Births)	Odds Ratio for Stillbirth (95% CI)*
Live birth			
Infant not small for gestational age			
≥37 wk of gestation†	370,541	892 (2.4)	1.0
32–36 wk of gestation‡	19,128	51 (2.7)	1.1 (0.8–1.5)
<32 wk of gestation	2,012	12 (6.0)	2.5 (1.4–4.4)
Infant small for gestational age			
≥37 wk of gestation	11,656	56 (4.8)	2.0 (1.5–2.6)
32–36 wk of gestation‡	1,991	19 (9.5)	4.0 (2.5–6.3)
<32 wk of gestation	735	14 (19.0)	8.0 (4.7–13.7)
Missing data	2,116	4	
Stillbirth	1,842	14 (7.6)	3.2 (1.9–5.4)
Total	410,021	1062 (2.6)	

* CI denotes confidence interval.

† The women in this group served as the reference group.

‡ The interval covered 32 weeks 0 days through 36 weeks 6 days of completed gestation.

not small for gestational age to 19.0 per 1000 among women whose first child was very preterm and was small for gestational age at birth (Table 1). As compared with women whose first child was born at term and was not small for gestational age, women whose first child was very preterm and was not small for gestational age had a significantly increased risk of stillbirth during their second pregnancy. The birth of a first infant who was small for gestational age was also associated with an increased risk of stillbirth during the second pregnancy, and the risk increased with decreasing gestational age. As expected, there was also a tendency for repeated stillbirths in successive births (Table 1).

The rates of antepartum hemorrhage and hypertension during the second pregnancy were 1.5 percent and 2.3 percent, respectively. As compared with women without antepartum hemorrhage during the second pregnancy, women with antepartum hemorrhage had a crude odds ratio for stillbirth of 9.0 (95 percent confidence interval, 7.4 to 10.8). As compared with women without hypertension during the second pregnancy, women with hypertension had a crude odds ratio for stillbirth of 1.5 (95 percent confidence interval, 1.1 to 2.1). As compared with lean women (a body-mass index of less than 20.0), women with higher body-mass indexes

had increased crude odds ratios for stillbirth during the second pregnancy as follows: 1.4 (95 percent confidence interval, 1.0 to 1.9) among those with a normal body-mass index (20.0 to 24.9), 1.9 (95 percent confidence interval, 1.3 to 2.7) among those who were overweight (body-mass index, 25.0 to 29.9), and 2.3 (95 percent confidence interval, 1.5 to 3.6) among those who were obese (body-mass index, 30.0 or more). As previously reported, advanced maternal age (35 years or older), a non-Nordic country of birth, maternal smoking, and short (0 to 3 months) or long (72 months or more) interpregnancy intervals also increased the risk of stillbirth.²

Since reproductive history as well as maternal factors and pregnancy complications influenced the risk of stillbirth, we examined the associations between maternal risk factors in the second pregnancy and the outcome of the first birth. As compared with women whose first child was born at term and was not small for gestational age, women whose child was born preterm, was small for gestational age, or was stillborn generally had a higher prevalence of maternal risk factors and complications during the second pregnancy (Table 2).

As compared with women whose first infant was not small for gestational age and was delivered

Table 2. Distribution of Maternal Characteristics and Complications during the Second Pregnancy, According to the Outcome of the First Pregnancy.

Outcome of First Pregnancy	Maternal Characteristics							
	Age ≥35 Years	Daily Smoker	Non-Nordic Country of Birth	Overweight*	Hypertensive Disease†	Antepartum Hemorrhage‡	Interpregnancy Interval 0–3 mo§	Interpregnancy Interval ≥72 mo§
<i>percentage of women</i>								
Live birth								
Infant not small for gestational age								
≥37 wk of gestation	8.1	19.2	6.7	28.7	2.0	1.5	1.4	3.2
32–36 wk of gestation	8.3	20.5	6.4	29.9	5.3	2.0	2.3	3.7
<32 wk of gestation	11.0	25.3	8.1	33.9	8.5	3.2	6.7	4.3
Infant small for gestational age								
≥37 wk of gestation	10.7	32.5	10.3	25.0	3.6	1.8	2.1	3.7
32–36 wk of gestation	11.2	29.1	6.7	31.4	13.1	2.9	4.3	4.3
<32 wk of gestation	13.5	22.6	8.0	33.2	26.3	4.4	8.7	4.0
Stillbirth	9.8	23.5	9.5	39.5	5.4	3.4	31.9	0.7

* Overweight was defined by a body-mass index of 25.0 or more.

† Hypertensive disease includes chronic hypertension, gestational hypertension, preeclampsia, and eclampsia.

‡ Antepartum hemorrhage includes placental abruption, placenta previa, and other reasons for antepartum bleeding.

§ The interpregnancy interval was calculated as the number of months between the birth of the first child and the estimated date of conception of the second child.

at term, women whose first infant was not small for gestational age but was delivered very preterm (before 32 weeks of gestation) had an adjusted risk of stillbirth in the subsequent birth of 2.2 (Model 1 in Table 3). The delivery of a first infant at term who was small for gestational age was also associated with an increased risk of stillbirth (odds ratio, 2.1), whereas the delivery of a first infant who was small for gestational age and moderately or very preterm increased the risk of stillbirth by factors of 3.8 and 6.3, respectively. When we also adjusted the analyses for maternal body-mass index and height during the second pregnancy (information that was available only from 1992 onward), delivery of a first very preterm infant who was not small for gestational age was no longer significantly associated with an increased risk of stillbirth, whereas the other results remained essentially unchanged (data not shown).

Because pregnancy complications may lead to fetal growth restriction as well as stillbirth, we also included hypertensive diseases and antepartum hemorrhage during the second pregnancy as covariates. In this model, the risks of stillbirth related to previous preterm small-for-gestational-age births were attenuated but remained significantly increased (Table 3). Finally, when we also included information about hypertensive diseases and antepartum hemorrhage during the first pregnancy, the odds of stillbirth among women whose first child was very preterm and was small for gestational age were attenuated but were still significantly increased (adjusted odds ratio, 4.1; 95 percent confidence interval, 2.0 to 8.2); the other risk estimates were materially unchanged and remained significant (data not shown).

When the analyses were stratified according to preterm and term stillbirth, we found that previous adverse pregnancy outcomes were primarily associated with an increased risk of preterm stillbirth (Table 4). As compared with women whose first infant was born at term and was not small for gestational age, women whose first child was very preterm and was small for gestational age had a risk of preterm stillbirth during their subsequent pregnancy of 5.9. A history of a previous stillbirth almost quadrupled the risk of preterm stillbirth in the subsequent delivery, but it was not associated with an increased risk of term stillbirth. Only previous very preterm and term small-for-gestational-age births increased the risk of term stillbirth during the subsequent pregnancy.

Previous adverse pregnancy outcomes were as-

Table 3. Association between the Outcome of the First Pregnancy and the Adjusted Odds Ratios for Stillbirth during the Second Pregnancy.*

Outcome of First Pregnancy	Odds Ratio for Stillbirth (95% CI)	
	Model 1†	Model 2‡
Live birth		
Infant not small for gestational age		
≥37 wk of gestation§	1.0	1.0
32–36 wk of gestation	1.1 (0.8–1.5)	1.0 (0.8–1.4)
<32 wk of gestation	2.2 (1.1–4.2)	2.0 (1.0–3.8)
Infant small for gestational age		
≥37 wk of gestation	2.1 (1.6–2.8)	2.1 (1.6–2.8)
32–36 wk of gestation	3.8 (2.3–6.3)	3.4 (2.1–5.6)
<32 wk of gestation	6.3 (3.2–12.2)	5.0 (2.5–9.8)
Stillbirth	2.8 (1.5–5.2)	2.5 (1.4–4.7)

* Both analyses were based on 877 cases of stillbirth. CI denotes confidence interval.

† Analyses were adjusted for mother's smoking status, mother's age, mother's level of education, family situation (living with or without the baby's father), mother's country of birth, year of second delivery, and interpregnancy interval.

‡ Analyses were adjusted for the covariates in Model 1 as well as for the presence or absence of hypertensive diseases and antepartum hemorrhage during the second pregnancy.

§ The women in this category served as the reference group.

sociated with increased risks of delivery of a stillborn infant who was small for gestational age (i.e., a stillborn fetus classified as being small for gestational age at delivery), and the risk was particularly increased among women whose first infant was both small for gestational age and preterm (Table 5). As compared with women whose first child was born at term and was not small for gestational age, women whose first child was small for gestational age and was moderately or very preterm had a risk of delivering a small-for-gestational-age stillborn second child of 8.0 and 15.2, respectively.

DISCUSSION

We found that the delivery of a first infant who was small for gestational age increased the subsequent risk of stillbirth. When the first infant was small for gestational age as well as preterm, the association with subsequent stillbirth was further amplified, and the risk increased with decreasing gestational age at delivery.

The strong association between the birth of a first infant who was small for gestational age and the subsequent risk of stillbirth may be explained by the fact that similar factors may underlie the two

Table 4. Association between the Outcome of the First Pregnancy and the Adjusted Odds Ratios for Preterm (before 37 Weeks of Gestation) and Term (37 Weeks of Gestation or More) Stillbirth during the Second Pregnancy.*

Outcome of First Pregnancy	Outcome of Second Pregnancy			
	Stillbirth <37 Wk of Gestation		Stillbirth ≥37 Wk of Gestation	
	no. (rate/ 1000 term births)	odds ratio (95% CI)	no. (rate/ 1000 term births)	odds ratio (95% CI)
Live birth				
Infant not small for gestational age				
≥37 wk of gestation†	439 (1.2)	1.0	453 (1.3)	1.0
32–36 wk of gestation	38 (2.0)	1.6 (1.1–2.3)	13 (0.8)	0.6 (0.3–1.1)
<32 wk of gestation	10 (5.0)	3.0 (1.4–6.4)	2 (1.3)	1.2 (0.3–4.7)
Infant small for gestational age				
≥37 wk of gestation	29 (2.5)	2.4 (1.6–3.5)	27 (2.5)	1.8 (1.2–2.8)
32–36 wk of gestation	14 (7.0)	5.4 (3.1–9.5)	5 (3.0)	1.6 (0.5–5.0)
<32 wk of gestation	10 (13.7)	5.9 (2.5–13.6)	4 (7.1)	5.0 (1.6–15.9)
Stillbirth	11 (6.0)	3.8 (1.9–7.6)	3 (1.8)	1.1 (0.3–4.6)

* Analyses were adjusted for mother's smoking status, mother's age, mother's level of education, family situation (living with or without the baby's father), mother's country of birth, year of second delivery, interpregnancy interval, and presence or absence of hypertensive diseases and antepartum hemorrhage during the second pregnancy. The multivariate analyses of preterm stillbirth and term stillbirth are based on 446 and 431 cases of stillbirth with complete information on covariates, respectively. CI denotes confidence interval.

† The women in this category served as the reference group.

conditions. Intrauterine malnourishment may lead to a liveborn small-for-gestational-age infant²⁴ or a stillbirth,²⁵ and many stillborn infants are classified as being small for gestational age at birth.^{4,5} Since women with a first small-for-gestational-age infant tend to have subsequent infants who are also small for gestational age,^{26,27} it was not surprising that a history of a small-for-gestational-age live birth increased the risk of a small-for-gestational-age stillbirth.

We found that the strength of the association between the live birth of a first small-for-gestational-age infant and the subsequent risk of stillbirth increased if the first infant was preterm (delivered before 37 completed weeks of gestation), especially if the first infant was delivered very preterm (before 32 weeks of gestation). Our definition of small size for gestational age was based on the Swedish fetal growth curve, which was developed to establish norms for intrauterine weight at different gestational ages.²² As compared with traditional birth-weight curves, fetal growth curves indicate that preterm infants are more likely than term infants to be small for gestational age and to have severe fetal growth restriction.^{19,20} The majority of preterm infants who are small for gestational age are delivered

electively,^{19,20} primarily because of signs of fetal growth restriction or asphyxia.²⁸ Since severe fetal growth restriction is closely associated with the preterm delivery of either a liveborn^{19,20,29} or stillborn^{1,5} infant who is small for gestational age, we speculate that some preterm infants who are small for gestational age would have been stillborn if they had been delivered at term.

The mechanisms accounting for the relations among the birth of a small-for-gestational-age infant, preterm birth, and the risk of a subsequent stillbirth are not clear. We controlled for maternal smoking status, one of the strongest risk factors for fetal growth restriction,¹³ as well as other maternal characteristics, such as body-mass index and level of education. When we also included information about maternal hypertensive diseases and antepartum bleeding as covariates, the risks were attenuated but remained significantly increased. Intergenerational research suggests that there may be genetic determinants of reproductive outcomes.³⁰ Genetic or environmental factors that contribute to the development of fetal growth retardation and intrauterine asphyxia not only may lead to an increased risk of having subsequent infants who are small for gestational age or stillborn, but also may explain the as-

Table 5. Association between the Outcome of the First Pregnancy and the Adjusted Odds Ratios for Delivery of a Stillborn Second Infant Who Was or Was Not Small for Gestational Age.*

Outcome of First Pregnancy	Outcome of Second Pregnancy			
	Stillborn Infant Who Was Small for Gestational Age		Stillborn Infant Who Was Not Small for Gestational Age	
	no. (rate/1000 births)	odds ratio (95% CI)	no. (rate/1000 births)	odds ratio (95% CI)
Live birth				
Infant not small for gestational age				
≥37 wk of gestation†	184 (0.5)	1.0	692 (1.9)	1.0
32–36 wk of gestation	16 (0.8)	1.6 (0.9–2.8)	34 (1.8)	0.9 (0.6–1.3)
<32 wk of gestation	4 (2.0)	3.1 (1.0–9.9)	8 (4.0)	1.7 (0.8–3.9)
Infant small for gestational age				
≥37 wk of gestation	20 (1.7)	3.8 (2.4–6.1)	34 (2.9)	1.6 (1.1–2.3)
32–36 wk of gestation	8 (4.0)	8.0 (3.9–16.5)	11 (5.5)	2.2 (1.1–4.5)
<32 wk of gestation	9 (12.3)	15.2 (6.4–35.8)	5 (6.9)	2.2 (0.7–7.0)
Stillbirth	3 (1.6)	3.2 (1.0–10.4)	10 (5.4)	2.5 (1.2–5.1)

* Analyses were adjusted for mother's smoking status, mother's age, mother's level of education, family situation (living with or without the baby's father), mother's country of birth, year of second delivery, interpregnancy interval, and presence or absence of hypertensive diseases and antepartum hemorrhage during the second pregnancy. The multivariate analyses of stillborn infants who were small for gestational age and stillborn infants who were not small for gestational age are based on 206 and 655 cases of stillbirth with complete information on covariates, respectively. CI denotes confidence interval.

† The women in this category served as the reference group.

sociation between the delivery of a previous small-for-gestational-age infant and the risk of stillbirth in subsequent pregnancies.

The rate of stillbirth during the second pregnancy was lower among women whose first infant had been stillborn (7.6 per 1000 births) than among women whose first infant had been very or moderately preterm and small for gestational age (19.0 per 1000 and 9.5 per 1000, respectively). Stillbirth has a heterogeneous cause, and the small number of repeated stillbirths did not allow us to subclassify them. Since the risk of recurrent stillbirth is well known,^{14,15} there is probably heightened supervision of women with a history of stillbirth. However, although the decline in stillbirth rates during the past three decades³¹ coincides with the introduction of diagnostic tools intended to increase fetal surveillance, it is not clear whether heightened supervision of women with previous stillbirths reduces the risk of recurrent stillbirth.

The strengths of our study include the small amount of missing data and the inclusion of virtually all births in Sweden during the study period. We adjusted for maternal factors and pregnancy complications related to stillbirth. Since some of the

factors we adjusted for, such as smoking and placental abruption and hypertensive disease, are also known causes of small size for gestational age,^{10,24} these adjustments may have led to an underestimation of the relation between the delivery of a first infant who was small for gestational age and the subsequent risk of stillbirth. Our analysis also controlled for the maternal level of education; however, because maternal stress and socioeconomic status have been linked to preterm birth³² as well as stillbirth,³³ there may be some residual confounding related to unmeasured social factors.

We were restricted to data included in the Swedish Birth Register and could not investigate previous pregnancy outcomes in relation to the underlying causes of stillbirth. Another limitation of this study is the use of small size for gestational age as a proxy for fetal growth restriction. Some infants classified as being small for gestational age will be small for reasons that are not related to fetal growth restriction, whereas other infants with a genetic disposition to be large may appear to be within the normal range, even though their growth has been restricted.⁵ For stillbirths, gestational age and birth weight were estimated at the time of delivery and not at the

time of death, which may have led to falsely high rates of stillbirth classified as small for gestational age or term. However, most stillbirths in Sweden are delivered within 24 hours after the diagnosis,³⁴ and a U.S. study of fetal histologic findings and stillbirth estimated that 80 percent of all stillbirths were delivered within one week after intrauterine death.³⁵ Thus, the influence of this potential misclassification is probably minimal. The Swedish Birth Register includes information only on stillbirths that occur at or after 28 weeks of gestation, and our results should not be generalized to include fetal deaths that occur before 28 weeks of gestation. Although many of the odds ratios we report are large, it should be kept in mind that the rates and absolute risks of stillbirth during a second pregnancy are still quite low, and the overwhelming majority of women

whose first infant was small for gestational age delivered liveborn second infants.

The strong association between the birth of a first infant who was small for gestational age and the subsequent risk of stillbirth further emphasizes the central role of fetal growth restriction in the etiologic process of stillbirth. Randomized, controlled trials have shown that the use of umbilical-artery Doppler velocimetry reduces the risk of perinatal mortality in high-risk pregnancies.³⁶ Early recognition of fetal growth restriction may be a prerequisite to the prevention of some stillbirths, but we do not yet know the optimal clinical approach to the compromised, very-preterm fetus with growth restriction.²⁹

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