Original Research

Risk of Recurrent Stillbirth in Subsequent Pregnancies

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OBJECTIVE: To compare the prospective risk of stillbirth between women with and without a stillbirth in their first pregnancy.

METHODS: We conducted a cohort study using perinatal data from Finland, Malta, and Scotland. Women who had at least two singleton deliveries were included. The exposed and unexposed cohorts comprised women with a stillbirth and live birth in their first pregnancy, respectively. The risk of stillbirth in any subsequent pregnancy was assessed using a Cox proportional hazards model. Time-to-event analyses were conducted to investigate whether first pregnancy outcome had an effect on time to or the number of pregnancies preceding subsequent stillbirth.

RESULTS: The pooled data set included 1,064,564 women, 6,288 (0.59%) with a stillbirth and 1,058,276 with a live birth in a first pregnancy. Compared with women with a live birth, women with a stillbirth in the first pregnancy were more likely to have a subsequent stillbirth (adjusted hazard ratio [aHR] 2.25, 95% CI 1.86–2.72). For women with more than two pregnancies, the difference in risk of subsequent stillbirth between the two groups increased with the number of subsequent pregnancies. Maternal age younger than 25 years or 40 years and older, smoking, low socioeconomic status, not having a partner, pre-existing diabetes, preeclampsia, placental abruption, or delivery of a growth-restricted neonate in a first pregnancy were independently associated with subsequent stillbirth. Compared with women with a live birth in the first pregnancy, women with a stillbirth were more likely to have another pregnancy within 1 year. The absolute risk of stillbirth in a subsequent pregnancy for women with stillbirth and live birth in a first pregnancy were 2.5% and 0.5%, respectively.

CONCLUSION: Compared with women with a live birth in a first pregnancy, women with a stillbirth have a higher risk of subsequent stillbirth irrespective of the number and sequence of the pregnancies. Despite high relative risk, the absolute risk of recurrence was low.

(Obstet Gynecol 2022;139:31–40)
DOI: 10.1097/AOG.0000000000004626

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Each author has confirmed compliance with the journal's requirements for authorship.

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Financial Disclosure
Kathleen Lamont was awarded an Elphinstone scholarship from the university of Aberdeen, Scotland. In addition, money from an NHS Grampian endowment fund financed storage of data. Sohinee Bhattacharya reports that money was paid to their institution from the NHS Grampian Endowment fund, Medical Research Scotland, and the Wellcome Trust ISSF fund. Sohinee Bhattacharya's husband has coauthored previous publications based on a similar data set. He is the Head of School of Medicine, Medical Sciences and Nutrition at the University of Aberdeen where she is also employed. The other authors did not report any potential conflicts of interest.

ISSN: 0029-7844/22

Results from a systematic review and meta-analysis suggest that previous stillbirth is associated with an increased risk of stillbirth in a subsequent pregnancy.[1] Most studies included in the systematic review looked at first and second pregnancies. Some smaller studies included women with more than two pregnancies and these report conflicting results, likely because of low numbers and limited power to demonstrate a statistically significant difference.[2–5]

To investigate the risk of stillbirth recurrence, most studies in the literature use retrospective analysis methods, primarily logistic regression models that calculate the odds of having a previous stillbirth accounting for sociodemographic and clinical factors.[1] This approach is unable to predict prospective risk of future pregnancy outcomes at the time of the first stillbirth. Clinically, it is important to know prospectively what the risk of a subsequent stillbirth is at the time of the initial stillbirth and identify any modifiable factors that can mitigate that risk. We conducted a large cohort study to investigate how factors including the outcome of a first pregnancy (stillbirth or live birth), affect the risk of having a stillbirth in any subsequent pregnancy. We hypothesized that compared with women who had a previous live birth, women whose first pregnancy resulted in a stillbirth had an increased risk of stillbirth in any subsequent pregnancy.

METHODS

A multi-country, registry-based cohort study using individual participant data from perinatal databases in Finland, Malta, and Scotland was conducted. The study population included all women in each of these countries who had delivered at least two singleton births during the specified timeframe (Finland between 1987 and 2015, Malta 1999 and 2015, and Scotland 1981 and 2015). Because of differences in the definition of stillbirth between countries, the pooled data included singleton live births and stillbirths delivered at 22 or more completed weeks of gestation or with a birth weight of 500 g (Finland and Malta) and 24 or more completed weeks of gestation (Scotland). In each of the participating countries, unique identifiers were used to link pregnancies in the same woman. Women with multiples pregnancies were excluded. Women who had a stillbirth in a first pregnancy formed the exposed cohort; women who had a live birth formed the unexposed cohort. The primary outcome was the occurrence of stillbirth in any subsequent pregnancy.

After obtaining permissions from the data custodians of all three registries, a predetermined list of variables was requested and anonymized data were provided. Range and consistency data checks were conducted, inconsistencies discussed with relevant data custodians and clarified and corrected when necessary. Covariates were selected a priori based on clinical relevance and directed acyclic graphs. Potential confounders at baseline (at the first pregnancy) included maternal age (categorized as younger than 20, 20–24, 25–29, 30–34, 35–39, or 40 years and older), body mass index (BMI, calculated as weight in kilograms divided by height in meters squared, categorized as underweight [lower than 18.5], normal [18.5–24.9], overweight [25–29.9], and obese [30 or higher], socioeconomic position, smoking status during pregnancy, and marital status (categorized as married or cohabiting or in a registered partnership [legally affirmed partnership of same- or opposite-sex partners], and other [never married, separated, divorced, widowed]).

The exposed and unexposed groups of women were also compared with regard to occurrence of medical and obstetric conditions in the first pregnancy (defined as the presence of an appropriate International Classification of Diseases Ninth Revision [ICD-9] or Tenth Revision [ICD-10] diagnostic code). These included pre-existing diabetes, pre-existing hypertension, anemia, thyroid condition, asthma, urinary tract infection, epilepsy, threatened miscarriage, gestational diabetes, gestational hypertension, obstetric cholestasis, preeclampsia, placental abruption, placenta previa, antepartum hemorrhage, fetal growth restriction,[6] and gestational age at birth (defined as completed weeks of gestation), which was categorized as 22–28, 29–32, 33–36, 37–42, and 43 weeks of gestation or more.

The individual participant data were analyzed using a one-step approach – the preferred method for rare outcomes.[7] The proportions of maternal demographic variables, medical, and obstetric conditions were compared between the exposed and unexposed cohorts to identify potential confounders. Continuous variables were summarized using mean and SD or median and interquartile range, as appropriate. When the outcome was continuous and normally distributed, the student t test was used, and the χ^2 test used for categorical variables (Fisher exact test if the assumptions were not met). All hypothesis tests were two-tailed and significance levels were set at $P<.05$.

Finland (since 1991) and Scotland provided information on nonsmokers, ever or former smokers and smokers, Malta only on nonsmokers and smokers. Because the Maltese data set was very small in comparison with the other two, it was decided to use all three categories. For socioeconomic position, Finland provided information on the mother's occupational class; Scotland provided Carstairs socioeconomic deprivation scores derived from postcode of residence[8]; Malta provided information on maternal education. Indicators of socioeconomic position all measure aspects of inequality that may have consequences for health. As these tend to be correlated with each other, educational attainment has been used as a proxy measure for socioeconomic status.[9] A composite socioeconomic variable was created and categorized into low and high socioeconomic status. For Finland, we categorized upper–white-collar workers as high socioeconomic status and white-collar workers, blue-collar workers, and others as low socioeconomic status. For Malta, university-level education was categorized as high socioeconomic status and postsecondary or secondary education, primary, special, or no education as low socioeconomic status. For Scotland, Carstairs categories one and two were categorized as high socioeconomic status and categories three, four, and five as low socioeconomic status.

To conduct time-to-event analysis, an event variable indicating whether the woman had a stillbirth in any subsequent pregnancy and an indicator for the total number of pregnancies were calculated in each of the data sets. Two "time" variables were also included: the first to examine the interval in years to stillbirth in a subsequent pregnancy, the second to examine the interval in terms of the number of pregnancies to stillbirth in a subsequent pregnancy. Years to stillbirth in a subsequent pregnancy was derived by subtracting year of index pregnancy from the year of the subsequent stillbirth, all other births treated as censored. For each woman, the starting point was taken as the date of the index birth, whether a stillbirth (exposed group) or a live birth (unexposed group). Not all women in the study will experience the event (subsequent stillbirth). Kaplan-Meier curves were plotted to show the cumulative probability of no subsequent stillbirth for each group. To investigate the effect of independent risk factors, multivariable modeling was performed using Cox proportional hazards regression, adjusting for first pregnancy outcome (live birth or stillbirth), maternal age, BMI, marital status, smoking status, socioeconomic status, pre-existing diabetes, pre-existing hypertension, preeclampsia, placental abruption, placenta previa, antepartum hemorrhage, fetal growth restriction, and gestational age at birth. Country was included in the model as a covariate, and for cross-country comparison, Scotland was chosen as the reference category. Adjusted hazard ratios (aHRs) and corresponding 95% CIs are presented, as are the absolute risk and the number needed to harm (NNH). The absolute risk is the difference in risk of stillbirth in a subsequent pregnancy between women with and without stillbirth in their first. The NNH indicates how many women on average need to be exposed to stillbirth in a first pregnancy for one woman to experience a subsequent stillbirth. Violation of the proportional hazards assumption was checked visually by comparing plots of the negative log of the Kaplan-Meier estimates of the survival function compared with the log of time.

We used multiple imputation[10] to impute missing values for BMI, smoking status, marital status, socioeconomic status, and gestational age at birth. A high proportion of data were missing for BMI and smoking status; however, we thought adjustment for these was important. Much smaller proportions of data were missing for the other variables. Missing values for these variables were created using multiple imputation by chained equations.[11] Logistic regression was used for imputing binary variables (marital status and deprivation category) and ordinal logistic regression for categorical variables (BMI, maternal age, and gestational age at birth). To improve accuracy of imputed values, year of birth (first pregnancy) was also included as an auxiliary variable. We created 20 imputed data sets[12] that were then combined for pooled estimates.[13] An analysis of complete cases (missing data were coded as "unknown") was also conducted. All statistical analyses were performed using SPSS 24 and Stata 13.0. Approval was sought and obtained from the relevant authorities in each of the countries (Scotland - Public Benefit and Privacy Panel for Health and Social Care, Ref: 1516-0309; Finland - Finnish Institute for Health and Welfare, No. THL/1719/5.05.00/2015; Malta - Directorate for Health Information and Research Malta, Miriam Gatt August 2016).

RESULTS

A total of 1,064,564 women had both first and subsequent pregnancies in the pooled data set during the study period. Of these, 6,288 (0.59%) women (2,437/512,267 [0.48%] in Finland, 122/17,624 [0.69%] in Malta, and 3,729/534,673 [0.70%] in Scotland) had a stillbirth in a first pregnancy (exposed group); the remaining 1,058,276 women (509,830 in Finland, 17,502 in Malta, and 530,944 in Scotland) had a live birth (unexposed group). Within the study population, 5,697 stillbirths occurred in subsequent pregnancies (2,423 in Finland, 96 in Malta, and 3,178 in Scotland). There were 157 recurrences of stillbirth. For women with stillbirth in a first pregnancy, the absolute risk of stillbirth in a subsequent pregnancy was 2.5% as compared with 0.5% for women who had a live birth (NNH=50). Over the timespan of the data, a downward trend was observed in stillbirth rates in Finland; in Scotland, stillbirth rates were fairly static until 2008, when a downward trend was also observed. Stillbirth rates in Malta did not change over time.

Table 1 shows univariable comparisons of maternal demographics and medical and obstetric conditions in the first pregnancy between the two comparison groups. Women in the exposed group were more likely to be younger than age 20 years or aged 30 years and older, to be overweight or obese, to smoke during pregnancy, to not live with a partner, to belong to lower socioeconomic status, to have pre-existing diabetes, to experience a threatened

Table 1. Comparison of First Pregnancy Maternal Characteristics Between Women With a Live Birth and Women With a Stillbirth

Pregnancy and Maternal Characteristics	Stillbirth (n=6,288)	Live Birth (n=1,058,276)	*P*
Maternal age (y)	26.10±5.66	25.60±4.93	**<.001**
Younger than 20	850 (13.5)	129,878 (12.3)	
20–24	1,745 (27.8)	313,549 (29.6)	
25–29	1,935 (30.8)	383,531 (36.2)	
30–34	1,241 (19.7)	188,528 (17.8)	
35–39	458 (7.3)	39,985 (3.8)	
40 or older	59 (0.9)	2,805 (0.3)	
BMI (kg/m²)	24.24 (21.46–28.71)	23.14 (20.96–26.23)	**<.001**
Underweight (lower than 18.5)	33 (3.2)	7,950 (3.7)	
Normal (18.5–24.9)	546 (53.0)	135,884 (63.2)	
Overweight (25–29.9)	248 (24.1)	46,934 (21.8)	
Obese (30 or higher)	203 (19.7)	24,171 (11.2)	
Not known	5,258	843,337	
Marital status			**<.001**
Married or cohabiting or legal partnership	3,831 (68.8)	751,567 (76.5)	
Other	1,739 (31.2)	230,648 (23.5)	
Not known	718	76,061	
Smoking status during pregnancy			**<.001**
Did not smoke	2,413 (69.6)	558,283 (79.3)	
Smoked	873 (25.2)	108,873 (15.5)	
Stopped or former smoker	181 (5.2)	36,894 (5.2)	
Not known	2,821	354,226	
Socioeconomic status			**<.001**
High	1,242 (20.3)	247,639 (23.9)	
Low	4,879 (79.7)	788,315 (76.1)	
Not known	167	22,322	
First antenatal visit at 12 wk or earlier			**<.001**
Yes	3,602 (65.5)	714,282 (70.9)	
No	1,895 (34.5)	293,340 (29.1)	
Not known	791	50,654	
Pre-existing diabetes			
No	6,203 (98.6)	1,053,614 (99.6)	
Yes	85 (1.4)	4,662 (0.4)	**<.001**
Pre-existing hypertension			
No	6,202 (98.6)	1,046,276 (98.9)	
Yes	86 (1.4)	12,000 (1.1)	.080
Anemia			
No	6,054 (96.3)	992,533 (93.8)	
Yes	234 (3.7)	65,743 (6.2)	**<.001**
Thyroid condition			
No	6,276 (99.8)	1,056,775 (99.9)	
Yes	12 (0.2)	1,501 (0.1)	.389
Asthma			
No	6,251 (99.4)	1,051,596 (99.4)	
Yes	37 (0.6)	6,680 (0.6)	.728
UTI			
No	6,164 (98.0)	1,036,005 (97.9)	
Yes	124 (2.0)	22,271 (2.1)	.493
Epilepsy			
No	6,266 (99.7)	1,054,633 (99.7)	
Yes	22 (0.3)	3,643 (0.3)	1.00
Threatened miscarriage			
No	6,158 (97.9)	1,047,768 (99.0)	
Yes	130 (2.1)	10,508 (1.0)	**<.001**

(*continued*)

Table 1. Comparison of First Pregnancy Maternal Characteristics Between Women With a Live Birth and Women With a Stillbirth (*continued*)

Pregnancy and Maternal Characteristics	Stillbirth (n=6,288)	Live Birth (n=1,058,276)	*P*
Gestational diabetes			
No	6,219 (98.9)	1,042,624 (98.5)	
Yes	69 (1.1)	15,652 (1.5)	**.014**
Gestational hypertension			
No	6,198 (98.6)	1,037,201 (98.0)	
Yes	90 (1.4)	21,075 (2.0)	**.002**
Obstetric cholestasis			
No	6,276 (99.8)	1,054,798 (99.7)	
Yes	12 (0.2)	3,478 (0.3)	.073
Preeclampsia			
No	6,044 (96.1)	1,021,785 (96.6)	
Yes	244 (3.9)	36,491 (3.4)	.064
Placental abruption			
No	5,755 (91.5)	1,055,271 (99.7)	
Yes	533 (8.5)	3,005 (0.3)	**<.001**
Placenta previa			
No	6,255 (99.5)	1,055,548 (99.7)	
Yes	33 (0.5)	2,728 (0.3)	**<.001**
Antepartum hemorrhage			
No	6,087 (96.8)	1,041,092 (98.4)	
Yes	201 (3.2)	17,184 (1.6)	**<.001**
FGR			
No	5,937 (94.4)	1,035,628 (97.9)	
Yes	351 (5.6)	22,648 (2.1)	**<.001**
Cord or hand prolapse			
No	6,191 (98.5)	1,051,789 (99.4)	
Yes	97 (1.5)	6,487 (0.6)	**<.001**
PROM			
No	6,207 (98.7)	1,034,145 (97.6)	
Yes	81 (1.3)	24,131 (2.3)	**<.001**
Mode of delivery			**<.001**
Unassisted vaginal	4,715 (75.9)	703,887 (66.6)	
Vaginal breech	781 (12.6)	4,928 (0.5)	
Forceps	207 (3.3)	92,447 (8.7)	
Vacuum	60 (1.0)	75,491 (7.1)	
Elective cesarean	33 (0.5)	39,812 (3.8)	
Intrapartum cesarean	413 (6.7)	140,146 (13.3)	
Not known	79	1,565	
Gestational age at birth (wk)			**<.001**
22–28	1,569 (25.1)	3,651 (0.3)	
29–32	1,109 (17.7)	7,303 (0.7)	
33–36	1,317 (21.0)	45,137 (4.3)	
37–42	2,238 (35.8)	995,576 (94.4)	
43 or more	24 (0.4)	3,339 (0.3)	
Not known	31		
Neonatal sex			**<.001**
Male	3,382 (54.1)	543,622 (51.4)	
Female	2,864 (45.9)	514,626 (48.6)	
Undetermined or not specified	42	28	

BMI, body mass index; UTI, urinary tract infection; FGR, fetal growth restriction; PROM, prelabor rupture of membranes.
Data are mean±SD, n (%), median (interquartile range), or n unless otherwise specified.
Bold indicates statistical significance.

miscarriage, and to develop preeclampsia, placenta previa, placenta abruption, or antepartum hemorrhage. Neonates born to women in the exposed group were more likely to be male and have growth restriction and were much more likely to be born preterm. Compared with women in the unexposed group, women in the exposed group were less likely to have anemia or to develop gestational diabetes or gestational hypertension.

A high proportion of data were missing for BMI (81.6%) and smoking status (39.2%). For the other imputed variables (marital status, socioeconomic status, and gestational age at birth), less than 10% were missing. We found that women who had a stillbirth were more likely to have missing information. We also found that women who had information missing for BMI, whether they had a live birth or a stillbirth, were also more likely to have information missing on smoking during pregnancy. Compared with women who had a live birth in their first pregnancy, women who had a stillbirth were less likely to attend their first antenatal appointment at 12 weeks of gestation or earlier. As information on BMI and smoking is recorded at the first antenatal appointment (between 8 and 12 weeks pregnant), this may provide some explanation why women with a stillbirth were more likely to have missing information. Missing data patterns are presented in Appendix 1, available online at http://links.lww.com/AOG/C509.

Figure 1 shows Kaplan-Meier curves for time to subsequent stillbirth for the exposed and unexposed groups. Figure 2 shows time-to-event analysis for the number of pregnancies to subsequent stillbirth for the exposed and unexposed groups. In Figure 1, the curves show that compared with women who had a live birth in their first pregnancy, women who had a stillbirth were more likely to have a subsequent stillbirth sooner, although in both groups this was still relatively rare. In Figure 2, the curves show that compared with women who had a live birth in their first pregnancy, for women who had a stillbirth, the risk of stillbirth increases with the number of subsequent pregnancies.

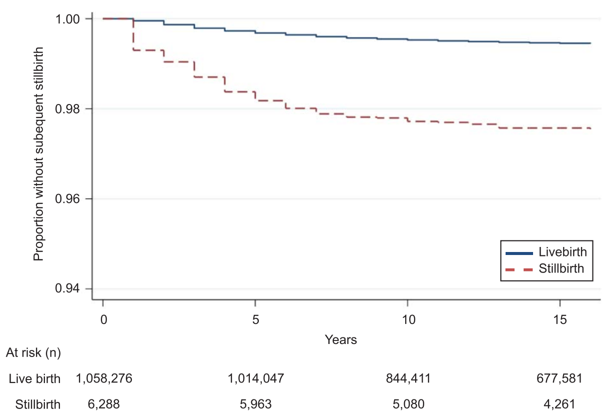

Fig. 1. Kaplan-Meier plot of time to stillbirth in any subsequent pregnancy by outcome of index pregnancy.

Lamont. Recurrent Stillbirth. Obstet Gynecol 2021.

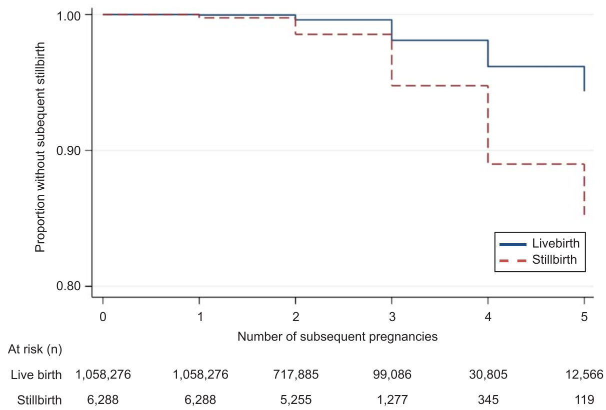

Fig. 2. Kaplan-Meier plot of the number of subsequent pregnancies to stillbirth in any subsequent pregnancy by outcome of index pregnancy.

Lamont. Recurrent Stillbirth. Obstet Gynecol 2021.

Table 2 provides adjusted hazard ratios for stillbirth in a subsequent pregnancy based on first pregnancy outcome and characteristics of the first pregnancy. After controlling for socio-demographic factors and obstetric conditions, stillbirth in a first pregnancy significantly increased the risk of subsequent stillbirth (aHR 2.25, 95% CI 1.86–2.72). Compared with women in Scotland, women in Finland and Malta were at increased risk of subsequent stillbirth (aHR 1.08, 95% CI 1.01–1.15; and aHR 1.41, 95% CI 1.14–1.74, respectively).

Compared with those aged 25–29 years, the risk of subsequent stillbirth was significantly increased if women were younger than age 20 years (aHR 1.63, 95% CI 1.49–1.77), 20–24 years (aHR 1.25, 95% CI 1.16–1.33), or 40 years or older (aHR 1.68, 95% CI 1.09–2.58) at the first pregnancy. Women who smoked (aHR 1.12, 95% CI 1.03–1.21), did not live with a partner (aHR 1.20, 95% CI 1.11–1.29), or were of low socioeconomic status (aHR 1.14, 95% CI 1.06–1.22) in a first pregnancy were also at increased risk of subsequent stillbirth. Pre-existing diabetes (aHR 2.42, 95% CI 1.88–3.11), preeclampsia (aHR 1.27, 95% CI 1.12–1.44), and placental abruption (aHR 1.41, 95% CI 1.06–1.86) in a first pregnancy were all independently associated with subsequent stillbirth when compared with women who did not have these conditions.

Irrespective of a live birth or a stillbirth, women who had a growth-restricted newborn in their first pregnancy were at significantly increased risk of subsequent stillbirth (aHR 1.58, 95% CI 1.39–1.81). Compared with women whose first children were

Table 2. Adjusted Hazard Ratios for Stillbirth in Any Subsequent Pregnancy by First Pregnancy Outcome and Characteristics in Women in Finland 1987–2015, Malta 1999–2015, and Scotland 1981–2015

Maternal and Obstetric Characteristics	aHR	95% CI	*P* (Cox Regression)
1st pregnancy outcome			**<.001**
Stillbirth	2.25	1.86–2.72	
Live birth	1.00		
Country			
Scotland	1.00		
Finland	1.08	1.01–1.15	**.026**
Malta	1.41	1.14–1.74	**.001**
Maternal age (y)			
Younger than 20	1.63	1.49–1.77	**<.001**
20–24	1.25	1.16–1.33	**<.001**
25–29	1.00		
30–34	1.06	0.97–1.15	.193
35–39	1.08	0.93–1.27	.317
40 and older	1.68	1.09–2.58	**.019**
Marital status			
Married or cohabiting or legal partnership	1.00		
Other	1.20	1.11–1.29	**<.001**
Smoking status			
Did not smoke	1.00		
Smoked during pregnancy	1.12	1.03–1.21	**.006**
Stopped or former smoker	0.98	0.83–1.14	.754
Socioeconomic status			
High	1.00		
Low	1.14	1.06–1.22	**<.001**
Pre-existing diabetes			
No	1.00		
Yes	2.42	1.88–3.11	**<.001**
Pre-existing hypertension			
No	1.00		
Yes	1.04	0.83–1.31	.746
Preeclampsia			
No	1.00		
Yes	1.27	1.12–1.44	**<.001**
Placental abruption			
No	1.00		
Yes	1.41	1.06–1.86	**.016**
Placenta previa			
No	1.00		
Yes	1.13	0.73–1.75	.595
Antepartum hemorrhage			
No	1.00		
Yes	0.98	0.81–1.18	.811
FGR			
No	1.00		
Yes	1.58	1.39–1.81	**<.001**
Gestational age at birth (wk)			
22–28	2.91	2.37–3.58	**<.001**
29–32	2.63	2.22–3.12	**<.001**
33–36	1.48	1.33–1.65	**<.001**
37–42	1.00		
43 or more	0.89	0.56–1.42	.630

aHR, adjusted hazard ratio; FGR, fetal growth restriction.
Bold indicates statistical significance.

born at term (after 37 weeks of gestation), women with children born preterm (less than 37 weeks) were at significantly increased risk of subsequent stillbirth, the risk increasing as gestational age of the first birth decreased (aHR 1.48, 95% CI 1.33–1.65 for women with children born at 33–36 weeks of gestation; aHR

2.63, 95% CI 2.22–3.12 at 29–32 weeks of gestation; and aHR 2.91, 95% CI 2.37–3.58 at 22–28 weeks of gestation). Compared with women who did not have these conditions, women who had pre-existing hypertension, placenta previa or antepartum hemorrhage in their first pregnancy were not at increased risk of subsequent stillbirth.

When a complete case analysis was conducted in which missing data were coded as unknown, the interpretation of the results of the Cox model was similar (Appendix 2, available online at http://links.lww.com/AOG/C509).

DISCUSSION

In this large, population-based, multi-country cohort, we found that women with an initial stillbirth were twice as likely to have a subsequent stillbirth compared with women with a first live birth. For women with more than two pregnancies, the difference in risk of subsequent stillbirth between the two groups increased with the number of subsequent pregnancies. Smoking, being single, low socioeconomic status, diabetes, preeclampsia, and placental abruption in a first pregnancy were found to be independent risk factors for subsequent stillbirth. In comparison with women aged 25–29 years in their first pregnancy, women younger than age 25 years and women aged 40 years and older were at significantly increased risk of subsequent stillbirth. Women whose first pregnancy resulted in the delivery of a growth-restricted or preterm neonate were also at increased risk of having a subsequent stillbirth, the risk increasing with decreasing gestational age at first delivery.

Previous studies have focused on the first and second pregnancies, or first subsequent pregnancy after a stillbirth.[1] This study evaluates the prospective risk of stillbirth in any subsequent pregnancy. As parity increases, a smaller proportion of women contribute to the analysis, particularly in the exposed cohort. Because of this, we did not present stillbirth beyond the fifth pregnancy as the numbers at risk would be too low to be clinically meaningful. Nevertheless, the overall pattern remains consistent.

Strengths of this study are the multi-country, population-based approach and prospective analysis. Collaborative use of data allowed investigation of a rare outcome such as stillbirth recurrence where large numbers are needed to ensure sufficient statistical power. The cross-national design ensures generalizability to other high-income countries with similar health care structure and low stillbirth rates. Limitations include transition from ICD-9 to ICD-10 codes and possible coding and misclassification errors, for example delay in detecting stillbirth and subsequent intrauterine retention can result in overestimation of fetal growth restriction, residual confounding, and the large amount of data that were missing on key confounding variables such as maternal BMI. We used multiple imputation to maximize efficiency and compared results with a complete case analysis in which missing data were coded as unknown; results were similar. Lack of data on race and ethnicity and our inability to link the data set to cause of death data are additional limitations.

As in previous research, we found that smoking,[14,15] not living with a partner,[4] and low socioeconomic status[16] were independent risk factors for stillbirth in a subsequent pregnancy. Although maternal obesity is known to increase the risk of stillbirth,[15] we did not find BMI to be independently associated with an increased risk of stillbirth in a subsequent pregnancy. In high-income countries, smoking and obesity during pregnancy are modifiable risk factors that urgently need addressing.[15,17,18] Evidence shows that smoking cessation interventions can be effective.[19] Effectiveness of interventions for reducing weight in obese pregnant women is less clear.[20] Similarly a meta-narrative review[21] found very little research investigating what might work to reduce socioeconomic inequalities and stillbirth in the United Kingdom. Interventions targeted to reduce stillbirth in specific social groups or communities and studies that explore the interactions between risk factors within specific groups are needed.[21]

As found in other studies, placental abruption, fetal growth restriction, and diabetes were independently associated with subsequent stillbirth.[22,23] Previous research[23,24] has found that women with preterm birth, delivery of a small-for-gestational-age neonate, and preeclampsia in an initial pregnancy are at increased risk of stillbirth in a second pregnancy. These risk factors are confirmed in the current study to hold true for any subsequent stillbirth.

The tendency for preterm birth, preeclampsia, placental abruption, and fetal growth restriction to recur suggests common causal factors for stillbirth related to impaired placental function,[5,23–26] and the possibility that these conditions predispose to each other.[27] Lean and colleagues[28,29] provide evidence for a link between advanced maternal age and placental dysfunction. Older women are also more susceptible to fetal growth restriction, and placental dysfunction may be a potential mechanism.[29] Further studies are required to determine the factors in the aging environment that are altered and how they relate to placental function. Development of effective screening methods of the placenta to detect potential problems during pregnancy and targeted interventions may help prevent stillbirth.[30]

In conclusion, women with a stillbirth in their first pregnancy have more than double the risk of stillbirth in any subsequent pregnancy. Despite significantly raised relative risk, the absolute risk remains low. Better screening for placental dysfunction may help identify women at higher risk of stillbirth. Findings from this study also highlight the importance of counseling women regarding modifiable risk factors to improve pregnancy outcomes after a stillbirth.

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PEER REVIEW HISTORY

Received August 8, 2021. Received in revised form October 1, 2021. Accepted October 8, 2021. Peer reviews and author correspondence are available at http://links.lww.com/AOG/C510.