Original Research

Advanced Maternal Age and Stillbirth Risk in Nulliparous and Parous Women

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OBJECTIVE: To investigate the association between advanced maternal age and stillbirth risks in first, second, third, and fourth births or more.

METHODS: A population-based registry study including all women aged 25 years and older with singleton pregnancies at 28 weeks of gestation and later gave birth in Sweden from 1990 to 2011; 1,804,442 pregnancies were analyzed. In each parity group, the risk of stillbirth at age 30–34 years, 35–39 years, and 40 years and older compared with age 25–29 years was investigated by logistic regression analyses adjusted for sociodemographic factors, smoking, body mass index, history of stillbirth, and interdelivery interval. Also, two low-risk groups were investigated: women with a high level of education and nonsmoking women of normal weight.

RESULTS: Stillbirth rates increased by maternal age: 25–29 years 0.27%; 30–34 years 0.31%; 35–39 years 0.40%; and 40 years or older 0.53%. Stillbirth risk increased by maternal age in first births. Compared with age 25–29 years, this increase was approximately 25% at 30–34 years and doubled at age 35 years. In second, third, and fourth birth or more, stillbirth risk increased with maternal age in women with a low and middle level of education, but not in women with high education. In nonsmokers of normal weight, the risk in second births increased from age 35 years or older and in third births or more from age 30 years or older.

CONCLUSION: Advanced maternal age is an independent risk factor for stillbirth in nulliparous women. This age-related risk is reduced or eliminated in parous women, possibly as a result of physiologic adaptations during the first pregnancy.

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LEVEL OF EVIDENCE: II

Advanced maternal age and nulliparity have been identified as independent risk factors for stillbirth in high-income countries.[1] Studies investigating the association between advanced maternal age and stillbirth risk in different parity groups are, however, scarce. Older nulliparous women were at higher risk for stillbirth when compared with a merged group of all multiparous women[2–4] or with second births only,[5–7] but another study found that the age-related risk was independent of parity.[8]

The physiologic mechanisms explaining the association between advanced maternal age and stillbirth have mainly focused on placental aging and insufficiency.[8–10] Sclerotic lesions, which increase by age, may be one factor causing underperfusion and impaired flux of nutrients to the fetus, eventually leading to intrauterine fetal demise and stillbirth.[8] The effects of parity are likely to differ from those of advanced maternal age. Neonatal birth weight generally increases with parity with the greatest increase between first and second births.[11] One hypothesis is that the first pregnancy paves the way for sustainable and more extensive endovascular trophoblast invasion in parous women[12] with increased nonmuscular tissue in the uterine spiral arteries,[13] ultimately leading to decreased vascular resistance and increased blood flow in the uteroplacental arteries in the next pregnancy. This interpretation is supported by Doppler studies of the uterine artery, showing more notches[14,15] and higher resistance index[15] in nulliparous than in parous women.

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Considering that advanced maternal age and parity may affect pregnancy and the risk of stillbirth in different ways, it is important to explore the combined effect of these two factors. The aim of the present study was to investigate the associations between maternal age and risks of stillbirth in first, second, third, and fourth births or more using a large population-based cohort study.

MATERIALS AND METHODS

The study was based on data from the Swedish Medical Birth Register, which includes more than 98% of all births in Sweden and is validated annually against the National Population Register using the mother's and neonate's unique personal identification numbers.[16,17] Starting from the first antenatal visit, information is collected prospectively during pregnancy and delivery using standardized records. We included single births of women aged 25 years or older recorded in the Medical Birth Register from 1990 to 2011. Consequently, a woman could have contributed information about all her births, whereas others could have provided information about their last birth at the beginning of the observation period (1990) or their first birth in the end of the period (2011).

The total number of births in Sweden from 1990 to 2011 was 2,267,990, and after exclusion of women younger than 25 years, multiple births, and births less than 28 weeks of gestation, 1,804,459 pregnancies remained. Missing data on parity (n=17) left 1,804,442 pregnancies in the final sample. Information on antepartal and intrapartal stillbirths was available from 28 weeks of gestation. The best available estimate of gestational age was determined by a hierarchical method based on expected date of parturition according to ultrasonography and last menstrual period.[18] In Sweden, all women are offered ultrasound pregnancy dating, and expected date of delivery is calculated from ultrasound fetal measurements for 95% of women at 17 weeks of gestation or earlier.[19] There was no information on miscarriages or fetal chromosomal status.

Data on maternal age and parity were collected at delivery, and information about maternal height, weight, family situation (dichotomized as living with partner compared with not living with partner), country of birth (dichotomized as Sweden compared with not Sweden), and smoking habits (daily smoking in early pregnancy compared with not smoking) were recorded at the first antenatal visit, commonly at 8–12 weeks of gestation. The validity of smoking information has previously shown to be high.[20] Level of education (elementary school or less, high school, and college or university) was obtained by linkage to the nationwide Swedish Population and Education Register.[21] Body mass index (BMI, calculated as weight (kg)/[height (m)]^2) was calculated from the information on weight and height in early pregnancy and was categorized according to the World Health Organization as: underweight (BMI less than 18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9), and obesity (BMI 30.0 or greater).

Information about maternal diseases was classified according to the Swedish versions of the 9th and 10th Revisions of the International Classification of Diseases (ICD-9 and ICD-10, respectively) and included pregestational diabetes (insulin-dependent or noninsulin-dependent; ICD-9 codes 250 and 648A; ICD-10 codes E10–E14 and O240–O243), gestational diabetes (ICD-9 code 648W; ICD-10 code O244), pregestational hypertension (self-reported by check box at first antenatal visit or by ICD-9 codes 401–405, 642C, and 642H; or by ICD-10 codes 110–115, O10, and O11), and preeclampsia (including eclampsia; ICD-9 codes 642E–642G; ICD-10 codes O14 and O15). Small for gestational age (SGA) was defined as a birth weight more than 2 standard deviations below the mean for gestational age and sex according to the sex-specific Swedish reference curve for normal fetal growth.[22]

Each woman's history of stillbirth was based on a diagnosis of stillbirth in her previous birth in the data set. Interdelivery interval was calculated as the difference between the year of delivery in the index pregnancy and the previous pregnancy in the data set.

The independent variable was maternal age when having the first, second, third, and fourth birth or more. In each parity group, maternal age 25–29 years was used as the reference and was compared with maternal age 30–34 years, 35–39 years, and 40 years or older. The rationale for the choice of reference group was twofold. First, we assumed that age 25–29 years was an age when outcomes would be optimal,[23] considering that the distribution of stillbirth has been described as U-shaped with increased rates in both ends of the age distribution.[24] Second, previous Swedish studies suggest that women with socioeconomic risk factors for stillbirth are overrepresented not only in teenagers but also in women aged 20–24 years.[25] Age 25–29 years was also the age interval with the largest number of births during the 21-year period (younger than 20 years 2.0%; 20–24 years 15.8%; 25–29 years 33.4%; 30–34 years 31.8%; 35–39 years 14.2%; and 40 years or older 2.8%).

Pregnancies of nulliparous women (first births), para 1 (second births), para 2 (third births), and para 3 or more (fourth or more births) were analyzed separately (as four cross-sectional studies). Rates of stillbirths were calculated for each age group. The associations between maternal age and each outcome were investigated by logistic regression analyses in three models. Model 1 was adjusted for time using the 21 years from 1990 to 2011 as a continuous variable. Model 2 was adjusted for time and for possible confounding variables (education, country of birth, family situation, smoking, maternal height, BMI, history of stillbirth, and interdelivery interval) and represent the principal findings of the study. Model 3 explored possible explanations of the findings by adding possible mediating factors such as maternal morbidity (pregestational diabetes, gestational diabetes, pregestational hypertension, and preeclampsia), and SGA births.

The principal findings are presented stratified by level of education: low or medium (elementary school or less+high school) compared with high (college or university), because the logistic regression analyses showed an interaction effect between maternal age and education in second and third births. For the interpretation of our findings we also investigated the association between maternal age and stillbirth in a low-risk group of nonsmokers who were of normal weight or underweight (BMI 24.9 or less). For simplicity, this group is referred to as nonsmokers of normal weight (normal weight 97%, underweight 3%).

The statistical software package was IBM SPSS Statistics 22. The study was approved by the Regional Ethics Review Board in Stockholm, Stockholm (2013/731-31/1).

RESULTS

Table 1 shows the distribution of maternal characteristics and potentially mediating factors in first, second, third, and fourth births or more. Mean maternal age increased from 30 years in first births to 34 years in fourth or more births. Of the potentially confounding factors, the following increased with parity: low level of education, not being born in Sweden, smoking, and overweight or obesity. High level of education was most frequent in first births. The rates of stillbirth in the previous birth increased with increasing parity, indicating that having a stillbirth increased the probability of having a subsequent birth. Of the potentially mediating factors, pregestational diabetes, gestational diabetes, and pregestational hypertension increased with parity, whereas preeclampsia and neonates born SGA were most frequent in first births.

In the total sample, the distribution of stillbirth by maternal age differed in shape from the distribution of stillbirth by parity. The stillbirth rate increased almost continuously by age: 25–29 years 0.27%; 30–34 years 0.31%; 35–39 years 0.40%; and 40 years or older 0.53%. The distribution of stillbirth rate by parity was J-shaped with the lowest rate in second birth: first births 0.33%; second births 0.26%; third births 0.32%; and fourth or more births 0.46%. Figure 1A and B shows the adjusted odds ratios of stillbirth by maternal age and parity, respectively.

Analyses of stillbirth risk by maternal age in the four parity groups were stratified by education because we found a statistically significant interaction between maternal age and education in second and third births (first births $P=.24$; second births $P=.03$; third births $P=.03$; fourth or more births $P=.97$).

The effects of maternal age after adjustment for confounding factors are the principal findings of this study (model 2 in Table 2). In first births, the risk for stillbirth increased with maternal age regardless of the woman's education. In the births of low- or medium-educated women, the risk for stillbirth increased with maternal age also among parous women. Compared with the reference group (aged 25–29 years), the risk of stillbirth in second, third, and fourth or more births increased by approximately 25% at age 30–34 years and even more in the two subsequent age categories. In contrast, in highly educated parous women, increasing maternal age was not associated with increased stillbirth risks.

We further explored the effect of maternal age on stillbirth in a low-risk group of nonsmokers of normal weight (n=818,863 pregnancies). To optimize statistical power, women aged 35 years and older were merged into one group, and third births and more were all included in one group (Table 3). In the low-risk group of nonsmokers of normal weight, the risk of stillbirth increased with maternal age in first births. In second births, the risk of stillbirth was not increased at age 30–34 years, whereas the adjusted odds ratio (OR) at age 35 years or older just reached statistical significance (adjusted OR 1.27, confidence interval 1.01–1.59). In the merged group of third births and more, the risk of stillbirth also increased by maternal age. In these analyses based on nonsmokers of normal weight, education was still a statistically significant variable in the regression models in first and third or more births (first births: $P=.03$; second births: $P=.10$; third or more births: $P=.01$).

The analyses of mediating factors (Table 2, model 3) show that the odds of stillbirth were reduced after adjustment for maternal morbidity and SGA. This reduction was mainly explained by SGA. The reduction in risk was most pronounced in first births, reflecting that rates of SGA births were highest in first births. In highly educated women, the rates of SGA

Table 1. Maternal Characteristics and Potentially Mediating Factors in First, Second, Third, and Fourth Births or More

Maternal Characteristics	Birth No. First (n=674,626)	Second (n=695,493)	Third (n=298,650)	Fourth or More (n=135,668)
Maternal age (y)				
25–29	52.7	39.9	26.4	16.1
30–34	34.8	41.4	42.1	36.9
35–39	10.7	16.2	26.6	34.8
40 or older	1.8	2.5	5.0	12.2
	29.9±3.8	31.0±3.9	32.5±4.1	34.2±4.4
Education				
Elementary school or less	5.7	8.3	14.8	29.0
High school	40.9	47.2	49.2	46.8
College or university	51.0	43.0	34.1	19.6
Missing	2.5	1.5	1.8	4.6
Family situation				
Living with partner	89.0	91.4	89.7	86.3
Other family situation	4.6	2.6	4.1	7.1
Missing	6.4	6.0	6.3	6.5
Country of birth				
Sweden	84.4	84.0	80.5	69.2
Not Sweden	15.6	16.0	19.5	30.8
Smoking in early pregnancy				
No	85.9	85.1	80.5	74.2
Yes	8.5	9.7	14.4	20.2
Missing	5.6	5.2	5.1	5.4
Height (cm)	167±6.3	167±6.2	166±6.3	165±6.4
BMI (kg/m^2)				
Underweight	2.0	1.8	1.3	1.1
Normal weight	53.3	49.7	44.4	34.0
Overweight	16.9	19.1	20.5	24.0
Obese	6.2	7.6	9.1	14.4
Missing	21.6	21.8	24.7	26.5
History of stillbirth*				
First pregnancy		0.30		
Missing		20.4		
Second pregnancy			0.51	
Missing			28.3	
Third pregnancy				0.73
Missing				37.2
Interdelivery interval (y)*				
Between first and second birth		3.2±2.0		
Missing		20.4		
Between second and third birth			4.2±2.7	
Missing			28.3	
Between third and fourth birth				37.2±2.7
Missing				37.5
Potentially mediating factors†				
Pregestational hypertension	0.6	0.6	0.7	0.9
Preeclampsia	4.2	1.7	1.7	1.9
Pregestational diabetes	0.6	0.7	0.7	1.0
Gestational diabetes	0.8	0.9	1.2	2.1
Intrauterine growth restriction	3.4	1.5	1.6	2.1
Missing	0.3	0.2	0.2	0.3

BMI, body mass index.

Data are % or mean±standard deviation unless otherwise specified.

* Missing cases depending on how many of a woman's pregnancies were occurring from 1990 to 2011.

† χ^2 test: first compared with second births: pregestational hypertension (P=.14), others (P<.001); second compared with third births: pregestational diabetes (P=.002), preeclampsia (P=.40), others (P<.001); third compared with fourth or more births, first compared with third births, first compared with fourth or more birth and second compared with fourth or more births: all statistically significant at P<.001.

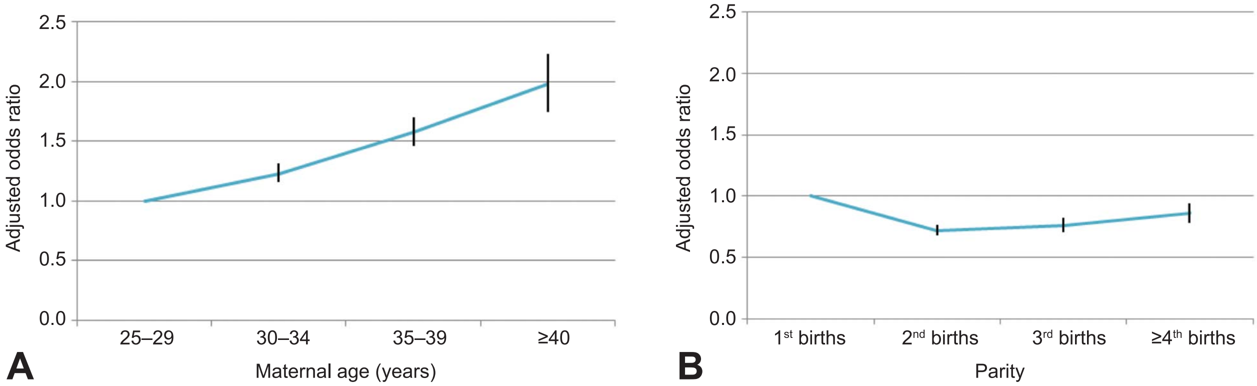

Fig. 1. A. Risk of stillbirth by maternal age, expressed as adjusted odds ratio with 95% confidence intervals. Logistic regression analysis adjusted for year of birth, parity, education, family situation, country of birth, smoking, maternal height, and body mass index. **B**. Risk of stillbirth by parity, expressed as adjusted odds ratio with 95% confidence intervals. Logistic regression analysis adjusted for year of birth, maternal age, family situation, country of birth, smoking, maternal height, and body mass index.

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were approximately 2.5 times higher in first births than in second, third, and fourth or more births (first births 3.0%; second births 1.2%; third births 1.2%; and fourth or more births 1.4%), and the same pattern was found in the low- or medium-educated group (figures not shown). Also, the age-related increase of SGA was most evident in first births with a continuous increase from 2.5% at age 25–29 years to 5.3% at age 40 years and older (high educated group). In the other three parity groups, the SGA rates were approximately 1% until age 35–39 years, when rates increased reaching 2% in the oldest age group of 40 years or older.

DISCUSSION

Advanced maternal age was associated with the highest risk of stillbirth in first births, the lowest in second births, and a possible increased risk in third births. This interpretation is supported by the findings of two low-risk groups (highly educated women and nonsmokers of normal weight) in which elimination of confounding factors was most optimal.

Flenady and colleagues[9] report that placental pathology was a major cause of stillbirth (29%) followed by infection (12%), cord complication (9%), maternal medical disorders (7%), congenital anomalies (6%), and intrapartum events (3%); no explanation was found in 30% of the 617 investigated cases of stillbirth. In the present study, we lacked information on possible causes of stillbirth. We found that maternal morbidity such as pregestational hypertension, preeclampsia, pregestational diabetes, and gestational diabetes had no or minor effect on age-related risk estimates; controlling for the effect of SGA reduced the age-related risk in first births and to some extent also in second and third births. Fetal growth restriction and stillbirth can both be related to defective placentation,[26] and some of the age-related effect on stillbirth risk may have been mediated through this mechanism.

That placental constraint may be one reason for the association between advanced maternal age and stillbirth risk is supported by an autopsy study of perinatal deaths. Naeye[8] found considerable indirect evidence that uteroplacental blood flow decreased by maternal age, because half of the perinatal deaths were associated with uteroplacental underperfusion, contributing to abruptio placentae, large placental infarcts, and placental growth restriction, all diagnoses that increase with maternal age. Sclerotic lesions in the myometrial arteries were identified as one possible cause of underperfusion. This conclusion was based on analyses of uteruses from 62 nonpregnant women who came to autopsy as a result of accidental death, and the proportion of such lesions increased from 11% at age 17–19 years to 83% after age 39 years. These age-related vascular changes did not differ by parity.

These findings may explain the overall effect of advanced maternal age on the risk of stillbirth, but not our finding that the age-related risk was primarily restricted to first births. Having experienced a first pregnancy may possibly improve the physiologic conditions for the second birth not only in terms of the softening and extension of tissues and muscles that contribute to the average shorter duration of labor in second births, but in a way that affects the fetal environment. One hypothesis could be that some of the effects of the hemodynamic changes that occur during the first pregnancy persist during the

Table 2. Stillbirth in Relation to Maternal Age in First, Second, Third, and Fourth or More Births Stratified by Level of Education

		Low or Medium Level of Education (n=993,937)*		
Maternal Age (y)	% (n)	Model 1	Model 2	Model 3
1st births				
25–29	0.34 (646)	Ref=1	Ref=1	Ref=1
30–34	0.44 (395)	1.31 (1.16–1.49)	1.28 (1.13–1.45)	1.20 (1.05–1.36)
35–39	0.57 (159)	1.69 (1.42–2.02)	1.56 (1.31–1.86)	1.37 (1.15–1.63)
40 or older	0.71 (33)	2.13 (1.49–3.02)	1.86 (1.31–2.65)	1.50 (1.05–2.15)
2nd births				
25–29	0.24 (478)	Ref=1	Ref=1	Ref=1
30–34	0.30 (408)	1.25 (1.10–1.43)	1.23 (1.08–1.41)	1.19 (1.04–1.36)
35–39	0.37 (171)	1.52 (1.27–1.81)	1.40 (1.17–1.68)	1.27 (1.06–1.52)
40 or older	0.55 (38)	2.27 (1.63–3.17)	1.98 (1.41–2.76)	1.72 (1.22–2.42)
3rd births				
25–29	0.27 (180)	Ref=1	Ref=1	Ref=1
30–34	0.34 (267)	1.26 (1.04–1.53)	1.25 (1.03–1.51)	1.19 (0.98–1.44)
35–39	0.50 (192)	1.92 (1.56–2.36)	1.87 (1.51–2.31)	1.70 (1.37–2.12)
40 or older	0.65 (46)	2.53 (1.83–3.51)	2.36 (1.68–3.30)	2.03 (1.44–2.85)
4th or more births				
25–29	0.39 (73)	Ref=1	Ref=1	Ref=1
30–34	0.47 (188)	1.22 (0.93–1.60)	1.25 (0.95–1.64)	1.20 (0.91–1.59)
35–39	0.51 (168)	1.31 (0.99–1.73)	1.34 (1.01–1.79)	1.26 (0.94–1.68)
40 or older	0.66 (70)	1.70 (1.22–2.37)	1.72 (1.22–2.43)	1.44 (1.02–2.05)

Ref, reference.

Data are adjusted odds ratio (95% confidence) unless otherwise specified.

Logistic regression analyses adjusted for: model 1: year of birth; model 2: year of birth, family situation (living with baby's father compared with not), country of birth (Sweden compared with not Sweden), smoking in early pregnancy, maternal height, body mass index, history of stillbirth in previous pregnancy, and number of years from previous to present birth; model 3: same as in model 2+maternal morbidity (pregestational diabetes, gestational diabetes, pregestational hypertension, preeclampsia) and intrauterine growth restriction (small for gestational age).

* The number of pregnancies was the same in each of the three models because missing values (Table 1) were imputed.

subsequent pregnancy and facilitates the blood transfusion to the next fetus. Doppler studies have reported changes in uterine arteries during the first pregnancy that persist into the second pregnancy. Hafner and colleagues[14] investigated uterine perfusion expressed as pulsatory index and "notching" of the uterine arteries. They found no statistical difference in pulsatory index values between women's first and second pregnancy, but an early diastolic notch was found more frequently in first pregnancies, suggesting that the decidual embedding of the trophoblast is less problematic in the second pregnancy. Prefumo and colleagues[15] found that parity had a significant effect on uterine artery resistance index and the prevalence of notching in the uterine artery flow waveforms and suggested that some permanent modification may persist in the maternal vessels after a successful pregnancy.

Other studies have investigated the effect of parity on structural changes in uterine spiral arteries. During normal placentation, trophoblastic cells infiltrate the thick-walled and muscular spiral arteries and transform them into thin-walled and floppy vessels that can dilate and accommodate to the increased uteroplacental blood flow necessary for a successful pregnancy.[27] Prefumo and colleagues[12] found more extensive invasion of endovascular trophoblastic invasion in parous women. Khong and colleagues[13] reported that nonmuscular tissues increased with increasing parity and suggested that these changes may modify subsequent vascular remodeling in the next pregnancy and provide an anatomical basis to explain the increasing birth weight with increasing parity, particularly of the second born.

Accordingly, it seems as if parity and advanced maternal age affect the risk of stillbirth in different and slightly opposite ways. If structural changes during the first pregnancy have a positive effect on placental perfusion during the second pregnancy, this could reduce the negative effects of the age-related vascular lesions. The positive effect may be limited in time and possibly negated by further effects of maternal aging on the vascular bed, and this could explain the observed trend in our study of an increased risk of stillbirth by maternal age in third births.

	High Level of Education (n=771,443)*		
% (n)	Model 1	Model 2	Model 3
0.22 (343)	Ref=1	Ref=1	Ref=1
0.27 (383)	1.26 (1.09–1.46)	1.23 (1.07–1.43)	1.17 (1.01–1.36)
0.44 (186)	2.02 (1.69–2.42)	1.86 (1.55–2.22)	1.63 (1.36–1.96)
0.67 (49)	3.12 (2.31–4.22)	2.72 (2.01–3.69)	2.29 (1.69–3.12)
0.23 (169)	Ref=1	Ref=1	Ref=1
0.21 (308)	0.95 (0.79–1.15)	0.94 (0.78–1.14)	0.94 (0.77–1.13)
0.28 (179)	1.29 (1.04–1.59)	1.18 (0.95–1.47)	1.14 (0.92–1.42)
0.28 (29)	1.32 (0.89–1.97)	1.12 (0.75–1.68)	1.00 (0.66–1.49)
0.23 (23)	Ref=1	Ref=1	Ref=1
0.25 (109)	1.13 (0.72–1.78)	1.18 (0.75–1.86)	1.13 (0.72–1.79)
0.25 (99)	1.18 (0.75–1.87)	1.23 (0.77–1.95)	1.12 (0.70–1.80)
0.29 (22)	1.42 (0.79–2.55)	1.41 (0.77–2.57)	1.19 (0.64–2.20)
0.34 (4)	Ref=1	Ref=1	Ref=1
0.34 (26)	1.01 (0.35–2.89)	1.08 (0.38–3.13)	1.70 (0.50–5.74)
0.35 (44)	1.05 (0.38–2.92)	1.12 (0.39–3.16)	1.73 (0.52–5.78)
0.42 (22)	1.23 (0.42–3.57)	1.29 (0.43–3.86)	1.93 (0.55–6.74)

Although the quality of data in the Swedish Medical Birth Register is high in terms of a low percentage of missing cases (2%), and linkage of data on perinatal deaths with the Swedish Population Register to optimize validity, the percentage of missing values was high in some of the confounding factors. The high rates were, however, largely explained by the time point at which the information started to be collected in the Swedish Medical Birth Register and by the way the study sample was defined (history of stillbirth and interdelivery interval) with information missing in women who had their previous birth before the onset of the data collection in 1990. Still, it cannot be excluded that the imputation of missing data into the regression analyses might have affected our findings. Also, we cannot exclude that some of the women born in other countries could have had a stillbirth before their arrival to Sweden without this history having been reported during their first pregnancy in the new country. Possible underreporting of previous stillbirths may have led to underestimation of number of parities and most in fourth or more births with the highest rate of migrant women.

Table 3. Stillbirth in Relation to Maternal Age in a Low-Risk Group of Nonsmokers of Normal Weight: First, Second, and Third or More Births

	Stillbirths In					
	First Births (n=341,759)		Second Births (n=323,744)		Third or More Births (n=153,355)	
Maternal Age (y)	n (%)	Adjusted OR (95% CI)	n (%)	Adjusted OR (95% CI)	n (%)	Adjusted OR (95% CI)
25–29	354 (0.20)	Reference	223 (0.18)	Reference	66 (0.21)	Reference
30–34	306 (0.25)	1.33 (1.14–1.56)	263 (0.19)	1.09 (0.90–1.31)	161 (0.25)	1.42 (1.06–1.91)
35 or older	145 (0.37)	1.96 (1.61–2.39)	138 (0.23)	1.27 (1.01–1.59)	154 (0.27)	1.61 (1.18–2.21)

OR, odds ratio; CI, confidence interval.
Number of pregnancies=818,863.
Logistic regression analyses adjusted for: first births: year of birth, education, family situation, country of birth, maternal height; second births: same as in first births+history of stillbirth in first birth and interval between first and second births; third or more births: same as in second births+history of stillbirth in second birth and interval between second and third births.

Despite the adjustment for many relevant confounding factors and stratification into low-risk groups, residual confounding may still be a problem. This may specifically be the case for women who deviated from the Swedish norm of having two children.[28,29] Women who had four births or more differed from women with other parities in terms of socioeconomic background and lifestyle (Table 1). When interpreting the age effect in fourth or more births, one also needs to take into account that the number of stillbirths in the reference group was very few (n=4). Together with probable unmeasured confounding and lack of statistical power, definite conclusions about the age effect in this group are hazardous.

In conclusion, our study suggests that advanced maternal age is an independent risk factor for stillbirth in nulliparous women. This age-related risk is reduced or eliminated in parous women, possibly as a result of physiologic adaptations during the first pregnancy.

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