

OBSTETRICS

Obesity and the risk of stillbirth: a population-based cohort study

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OBJECTIVE: Obesity is a known risk factor for stillbirth. However, this relationship has not been characterized fully. We attempted to further examine this relationship with a focus on delivery near and at term.

STUDY DESIGN: We designed a retrospective cohort study of singleton nonanomalous live births and stillbirths in the states of Washington and Texas to examine the associations of maternal prepregnancy body mass index (BMI) and risk of stillbirth. Confounder-adjusted hazard ratio of stillbirth in relation to BMI was estimated through Cox proportional hazards regression model. The hazard ratio was used to estimate the population-attributable risk. We also estimated the fetuses who were at risk for stillbirth based on gestational age.

RESULTS: Among 2,868,482 singleton births, the overall stillbirth risk was 3.1 per 1000 births ($n = 9030$). Compared with normal-weight women, the hazard ratio for stillbirth was 1.36 for overweight

women, 1.71 for class I obese women, 2.00 for class II obese women, 2.48 for class III obese women, and 3.16 for women with a BMI of ≥ 50 kg/m². The fetuses who are at risk for stillbirth increased after 39 weeks' gestation for each obesity class; however, the risk increased more rapidly with increasing BMI. Women with a BMI of ≥ 50 kg/m² were at 5.7 times greater risk than normal weight women at 39 weeks' gestation and 13.6 times greater at 41 weeks' gestation. Obesity was associated with nearly 25% of stillbirth that occurred between 37 and 42 weeks' gestation.

CONCLUSION: There is a pronounced increase in the risk of stillbirth with increasing BMI; the association is strongest at early- and late-term gestation periods. Extreme maternal obesity is a significant risk factor for stillbirth.

Key words: obesity, pregnancy, stillbirth, timing of delivery

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In the United States, 35.7% of adults are obese.¹ The prevalence of obesity has increased relentlessly over the last few decades, with the fastest rate of increase at the extreme end of the obesity range, that is, for categories of body-mass index (BMI) ≥ 40 and ≥ 50 kg/m². Data from self-reported telephone surveys, in which respondents are likely to understate their weight, show that the proportion of adults who admit to BMI ≥ 40 kg/m² was 3.1% in

★ EDITORS' CHOICE ★

2005 compared with 2.2% in 2001; the proportion of adults with BMI ≥ 30 kg/m² rose from 19.8-27.2%.²⁻⁵ Among pregnant women, obesity is also a growing health concern that is associated with numerous pregnancy-related complications.^{6,7} These include gestational diabetes mellitus, prepregnancy hypertension, gestational hypertension, venous thromboembolism, and

preeclampsia.^{8,9} Obesity is also associated with a delay in the onset of spontaneous labor and thus an increase in the interventions of labor induction and cesarean delivery.^{8,10-12}

Maternal obesity is also an established risk factor for stillbirth. The reported risk of stillbirth is 2–5 times higher in obese, compared with normal-weight, women.¹²⁻¹⁴ The risk of stillbirth that is associated with obesity increases with gestational age. Using a Danish birth cohort of >54,000 women, Nohr et al¹⁴ reported a hazard ratio (HR) for stillbirth at 20-27 weeks of 1.9 for women with BMI ≥ 30 kg/m² compared with women with normal BMI (18.5-24.9 kg/m²). The HR at 28-36 weeks' gestation was 2.1, at 37-40 weeks' gestation was 3.5, and at ≥ 41 weeks' gestation was 4.6. Epidemiologic studies have also demonstrated a strong dose-dependent association between BMI and stillbirth^{15,16}; the largest of these studies found that, among class III obese women (BMI, ≥ 40 kg/m²), the risk of stillbirth is 1.5-times higher compared with women with class I obesity (BMI, 30-34.9 kg/m²).¹⁵

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Data from multiple sources show that obese women are at higher risk of stillbirth the higher their BMI and the later the gestational age. However, important questions remain in the appropriate treatment of obese women in pregnancy to reduce their risk of stillbirth. In terms of determining the optimal gestational age for delivery, it is clear that the risk of stillbirth between each obesity class is different, so the timing of delivery should be different. The available evidence does not delineate these differences adequately to direct specific treatment guidelines for each obesity class. Therefore, we set out to quantify the relationship between obesity and stillbirth, week by week. Specifically, we were interested in calculating the risk of stillbirth for ongoing undelivered pregnancies at each gestational week. This rate can be compared directly with the published neonatal death rate (NDR) of the same gestational week as a way to estimate the overall change in perinatal mortality rates if a policy of delivery at a specific gestational week were to be instituted.

MATERIALS AND METHODS

Currently, there are no available national stillbirth databases in the United States that include maternal prepregnancy weight. Therefore, we queried all 50 states individually to identify state-level birth and stillbirth databases that contained this information. We initially identified 17 states with the desired information and excluded those with small delivery numbers, prohibitively high cost for access to data, or missing variables of interest. We used the vital records data from the states of Washington and Texas to examine the association between prepregnancy BMI and risk of stillbirth. Washington and Texas databases originate from birth and death certificates that are completed near the time of birth. To improve data quality, both birth and death certificates records are checked and edited for accuracy. For example, data value restrictions are placed on variables such as maternal age, and warnings are generated if maternal age is <14 or > 49 years. Both states perform routine, periodic data quality checks to identify facilities and providers with large amounts of missing data. In addition

to internal quality measures, the National Center for Health Statistics also conducts independent reviews of each state to verify data quality. To ensure future compliance, field visits are conducted when non-compliant sites are identified.

This study was approved by the Drexel University College of Medicine Institutional Review Board, and by the Departments of Public Health of Washington and Texas.

Analysis was limited to singleton pregnancies that delivered between 20 and 42 weeks' gestation, based on best clinical estimate of gestational age. The best clinical estimate of gestational dating, which incorporates data from other sources in addition to the last menstrual period, is considered superior to the menstrual-based estimate,¹⁷ which also is contained in the vital statistics data. Pregnancies with missing pregestational weight, height, or gestational age and those with maternal height recorded as <48 inches were removed from the cohort. Severe fetal anomalies that included anencephaly, spina bifida, cardiac anomalies, diaphragmatic hernia, gastroschisis, omphalocele, and chromosomal abnormalities were also removed. We excluded underweight women (BMI, <18.5 kg/m²) from analysis, because the primary objective of this study was to determine the effects of obesity on stillbirth risk.

For births in Washington, we abstracted data between 2003 and 2011 (n = 784,861 live births and 4735 stillbirths); for births in Texas, we abstracted data between 2006 and 2011 (n = 2,422,522 live births and 13,939 stillbirths). Of these births, we sequentially excluded 101,827 multiple births, 11,438 births with gestational age at delivery <20 or ≥43 weeks' gestation, 7937 births with severe anomalies, 86,744 births with missing covariate data, and 149,629 births to women with BMI <18.5 kg/m² or height <48 inches. After all exclusions, 2,868,482 singleton births (9030 stillbirths) remained for analysis (Figure 1). Nearly one-third of the stillbirths were excluded because of missing variables. We conducted a separate comparison of this group with those included for analysis to identify any selection bias within the data.

Maternal prepregnancy weight generally was self-reported by the woman and recorded by the prenatal care provider at the first prenatal visit. The care provider also recorded height at the first prenatal visit. BMI was defined as the ratio of maternal prepregnancy weight (in kilograms) over square of height (in meters). After the recommendations of the World Health Organization,¹⁸ we categorized BMI in the following manner: normal (18.5-24.9 kg/m²), overweight (25.0-29.9 kg/m²), obese class I (30.0-34.9 kg/m²), obese class II (35.0-39.9 kg/m²), and obese class III (40.0-49.9 kg/m²). We separately analyzed women with a BMI ≥50 kg/m². Obesity of this magnitude was once considered rare, but its prevalence has been increasing at a rapid rate.⁵ A growing body of evidence suggests that this group is at even higher risk of maternal and fetal complications than less severely obese women.¹⁹⁻²¹

We divided gestational age into 4 periods in the following manner: early preterm (30-33 weeks), late preterm (34-36 weeks), early term (37-39 weeks), and late term (40-42 weeks). We calculated the HR of stillbirth that was associated with obesity for each gestational period using Cox proportional hazards regression analysis. We estimated the confounder-adjusted HR of stillbirth in relation to BMI. Potential confounders considered for adjustment included maternal age (grouped as <20, 20-24, 25-29, 30-34, 35-39, and ≥40 years), parity, education (grouped as less than high school, high school diploma, and bachelor's degree or higher), no prenatal care, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and other race), and smoking. In addition, we also adjusted the analyses for chronic hypertension and pregestational diabetes mellitus. We calculated the population-attributable risk (PAR) using the adjusted HRs for each BMI class for the 4 gestational periods as described earlier.

Because at any given gestational age the fetus is at risk of stillbirth not only during that week but during the remaining weeks of gestation, we also estimated the risk of stillbirth for ongoing pregnancies based on gestational age with the following fraction:

No. of stillbirths for given week of gestation + all stillbirths that occurred thereafter
 All deliveries during and after the given week of gestation

RESULTS

In this cohort of >2.8 million women that delivered a singleton birth, 51.4% were normal weight; 26.0% were overweight; 13.1% were class I obese; 5.8% class II obese; 3.4% class III obese, and 0.4% had BMI ≥ 50 kg/m². Subject characteristics for each BMI class are listed in Table 1. On average, women with higher BMI at the start of pregnancy gained less weight, were older than those with lower BMI, and had achieved lower education levels. A higher proportion was black and multiparous, especially among the highest obesity classes. They were more likely to smoke and more likely to have diabetes mellitus and hypertensive disorders in pregnancy. Contrary to previous reports, obese women demonstrated a trend toward earlier delivery as BMI increased.

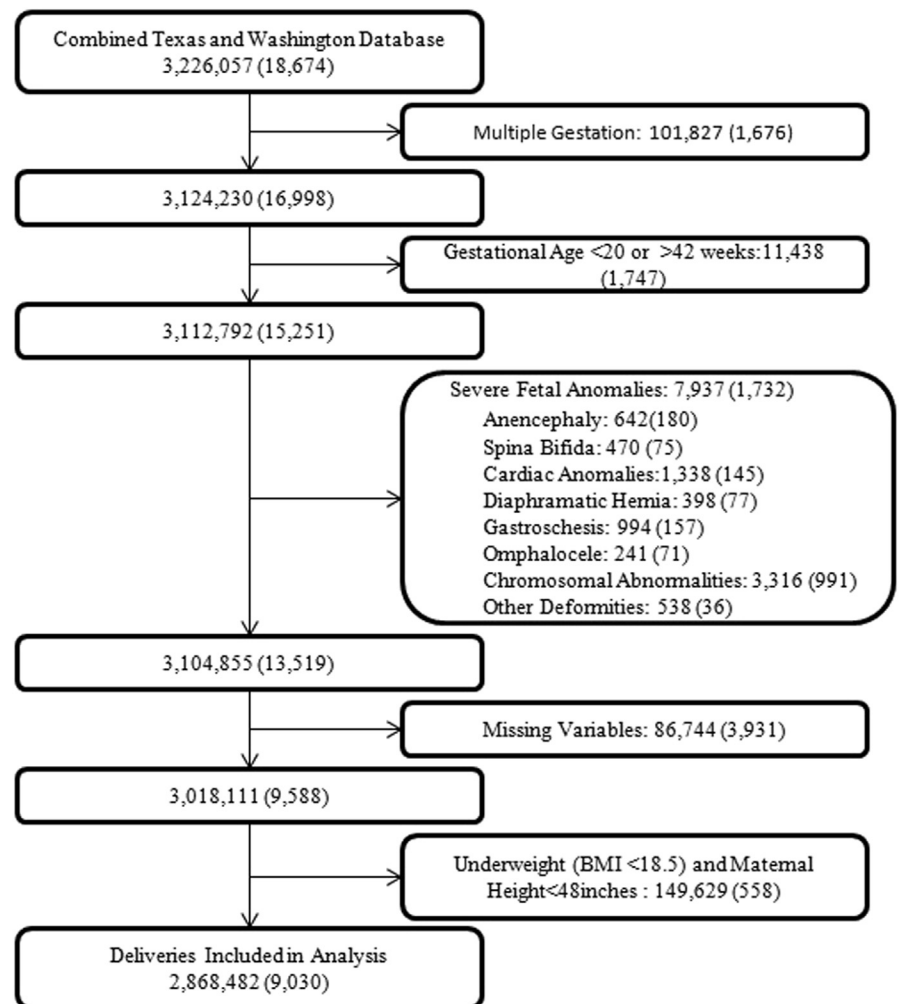
Among the stillbirth group who were excluded from analysis because of missing covariate data, the rate of exclusion was similar from Washington and Texas. Compared with stillbirths that were included in the analysis, women who were excluded were similar in age and smoking. A proportionally larger number of women who were excluded were black, had lower education, were multiparous, and delivered earlier (Table 2).

The HR for stillbirth that were associated with each obesity class and stratified by gestational periods is presented in Table 3 and Figure 2. At each gestational age epoch, the risk for stillbirth increased with increasing BMI. HR increased gradually with gestational age for overweight and class I and II groups from 1.25, 1.38, and 1.28 at 30-33 weeks to 1.33, 2.31, and 2.37 at 40-42 weeks, respectively. However, class III obese women and those with BMI ≥ 50 kg/m² exhibited a different pattern; instead of the gradual increase that is common to the less extreme classes, the HR sharply increased at the end of pregnancy. For these 2 groups, the HR of 1.40 and 1.69, which was seen at 30-33 weeks'

gestation, rose to 3.20 and 2.95 at 37-39 weeks' gestation and jumped to 3.30 and 8.95 at 40-42 weeks' gestation. The results are adjusted for other known risk factors that are associated with stillbirth, as described previously.

The PARs that were associated with obesity at each gestational period are presented in Table 4. The overall disease burden of stillbirth that is associated with obesity (BMI, ≥ 30 kg/m²) was 19.6%, but the PAR was significantly higher at term. From 37-39 weeks' gestation, 24.4% of stillbirths were associated with obesity, which increased to 28.4% at 40-42 weeks' gestation. The stillbirth risk that was associated with morbid obesity (BMI, ≥ 40 kg/m²) was 5.7% overall, 5.3%

FIGURE 1
Cohort composition



Results represented as all cases (stillbirth cases) from the combined Texas and Washington State databases with births that met the exclusion criteria sequentially eliminated. The final cohort for analysis included 9030 stillbirths among 2,868,480 singleton nonanomalous births.

BMI, body mass index.

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TABLE 1
Cohort characteristics

| Variable | Normal weight | Overweight | Class | | | Body mass index ≥ 50 kg/m ² |
|--|-------------------|-----------------|----------------------------------|-----------------------------------|-------------------------------------|---|
| | | | I (30.0–34.9 kg/m ²) | II (35.0–39.9 kg/m ²) | III (≥ 40 kg/m ²) | |
| Washington, n | 221,859 (40.4%) | 173,436 (31.6%) | 86,599 (15.8%) | 40,430 (7.4%) | 23,672 (4.3%) | 3123 (0.6%) |
| Texas, n | 1,252,048 (54.0%) | 571,770 (24.7%) | 287,805 (12.4%) | 125,971 (5.4%) | 72,600 (3.1%) | 9166 (0.4%) |
| Total, n | 1,473,907 (51.4%) | 745,206 (26.0%) | 374,404 (13.1%) | 166,401 (5.8%) | 96,272 (3.4%) | 12,289 (0.4%) |
| Characteristics | | | | | | |
| Average weight gain, lb ^a | 33.3 \pm 32.1 | 31.3 \pm 35.2 | 27.9 \pm 37.1 | 24.6 \pm 38.5 | 20.8 \pm 38.6 | 17.7 \pm 47.2 |
| Mean maternal age, y ^a | 26.6 \pm 6.2 | 27.3 \pm 6.1 | 27.5 \pm 5.9 | 27.7 \pm 5.8 | 28 \pm 5.6 | 28.8 \pm 5.4 |
| Height, in ^a | 63.9 \pm 2.8 | 63.7 \pm 2.9 | 63.6 \pm 2.9 | 63.8 \pm 3.0 | 63.9 \pm 3.1 | 63.6 \pm 3.4 |
| Race, % | | | | | | |
| White | 44.4 | 40.5 | 39.4 | 42.0 | 42.7 | 40.1 |
| Black | 8.4 | 10.1 | 11.1 | 12.6 | 15.7 | 22.2 |
| Hispanic | 39.4 | 44.3 | 45.6 | 38.7 | 38.7 | 35.1 |
| Other | 7.9 | 5.2 | 3.9 | 2.9 | 2.9 | 2.6 |
| Education, % | | | | | | |
| <12 y | 24.1 | 27.1 | 26.4 | 23.1 | 20.2 | 19.6 |
| High school diploma | 49.9 | 52.6 | 57.6 | 62.6 | 67.0 | 69.5 |
| \geq Bachelor's degree | 26.0 | 20.4 | 16.0 | 14.3 | 12.8 | 10.8 |
| Smoking, % | 8.3 | 8.5 | 9.5 | 10.1 | 11.0 | 10.5 |
| Primiparous, % | 42.1 | 33.9 | 30.4 | 29.8 | 29.9 | 29.3 |
| No prenatal care, % | 5.6 | 5.7 | 5.2 | 4.9 | 4.7 | 4.9 |
| Assisted fertility, % | 0.5 | 0.4 | 0.4 | 0.5 | 0.5 | 0.3 |
| Pregestational diabetes mellitus, % | 0.3 | 0.6 | 1.1 | 1.7 | 2.5 | 3.8 |
| Chronic hypertension, % | 0.5 | 0.9 | 1.7 | 2.8 | 4.6 | 8.8 |
| Gestational diabetes mellitus, % | 2.6 | 4.5 | 6.7 | 8.6 | 10.6 | 13.5 |
| Gestational hypertension, % | 3.4 | 4.9 | 6.7 | 8.7 | 10.5 | 13.4 |
| Gestational age at delivery, % (mean birthweight, g) | | | | | | |
| <30 wk | 0.8 (1095) | 0.9 (1060) | 1.1 (1009) | 1.3 (1025) | 1.6 (984) | 1.8 (1035) |
| 30–33 wk | 1.3 (1963) | 1.3 (1958) | 1.5 (1969) | 1.6 (1959) | 1.8 (1919) | 2.2 (1966) |
| 34–36 wk | 6.3 (2680) | 6.3 (2749) | 6.9 (2792) | 7.4 (2833) | 8.1 (2876) | 9.7 (2933) |
| 37–39 wk | 63.5 (3263) | 64.2 (3336) | 65.1 (3376) | 66.1 (3410) | 67 (3442) | 68.1 (3479) |
| 40–42 wk | 28.2 (3509) | 27.2 (3570) | 25.5 (3594) | 23.5 (3617) | 21.6 (3623) | 18.2 (3616) |

^a Data are given as mean \pm standard deviation.Yao. Obesity and the risk of stillbirth. *Am J Obstet Gynecol* 2014.

TABLE 2
Characteristics of stillbirths not included in analysis

| Variable | Included in the study | Missing variables |
|--------------------------------|-----------------------|-------------------|
| Washington, n | 2249 (70.1%) | 960 (29.9%) |
| Texas, n | 6781 (69.5%) | 2971 (30.5%) |
| Total, n | 9030 (69.7%) | 3931 (30.3%) |
| Characteristics | | |
| Maternal age, y ^a | 29.5 ± 7.5 | 29.2 ± 7.7 |
| Race, % | | |
| White | 39.1 | 28.8 |
| Black | 16.5 | 21.1 |
| Hispanic | 38.0 | 38.1 |
| Other | 6.4 | 12.0 |
| Education, % | | |
| <12 y | 75.0 | 83.8 |
| High school diploma | 16.1 | 10.1 |
| ≥Bachelor's degree | 9.0 | 6.1 |
| Smoking, % | 10.2 | 9.1 |
| Primiparous, % | 50.3 | 47.2 |
| Gestational age at delivery, % | | |
| <30 wk | 55.0 | 61.1 |
| 30-33 wk | 12.9 | 12.1 |
| 34-36 wk | 12.5 | 11.0 |
| 37-39 wk | 15.6 | 12.0 |
| 40-42 wk | 4.0 | 3.9 |

^a Data are given as mean ± standard deviation.

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at 37-39 weeks' gestation and 8.0% at 40-42 weeks' gestation.

The fetuses who were at risk for stillbirth for each gestational week are presented graphically in Figure 3, stratified by BMI class. For each obesity class, the fetuses who were at risk for stillbirth declined until 39 weeks' gestation and increased thereafter. There were no stillbirths reported at 42 weeks' gestation for 2 of the groups, which may reflect a general reluctance in practice to allow pregnancy to continue 2 weeks past the estimated date of delivery. Risk of stillbirth was higher throughout gestation with higher degrees of maternal obesity. This relationship was especially evident for the group with BMI >50 kg/m²; at 39 weeks' gestation, the group of fetuses who were at

risk for stillbirth was 5.7 times that of the normal weight group; at 41 weeks' gestation, the rate is 13.6 times higher.

COMMENT

This large, population-based cohort study comprising >2.8 million women reveals interesting data on the association between maternal prepregnancy BMI and stillbirth risk. First, we have illustrated a dose-response relationship between obesity and stillbirth throughout pregnancy, which is consistent with other reports.^{15,16} Additionally, our study showed that, although the dose-response relationship exists in every gestational period, the impact of obesity on risk of stillbirth is more pronounced at term. Although this finding echoes the

study reported by Nohr et al,¹⁴ our data show that extremely high BMI affects stillbirth differently compared with lower BMI. The rate at which risk for stillbirth increased for overweight and class I and II obese women are linear from 30-42 weeks' gestation (Figure 2). In contrast, among class III obese women and those with BMI >50 kg/m², the risks appear to be nonlinear with time; the risk of stillbirth escalates faster with increasing gestational age in these extreme classes. These findings remained consistent after adjustment for known confounding risk factors such as chronic hypertension and pregestational diabetes mellitus.

Our study further highlights the significant contribution obesity makes to stillbirth. Our data show that nearly 20% of all stillbirths in this population were associated with obesity, and at term—after 37 weeks' gestation—nearly 1 in 4 stillbirths were associated with obesity. These findings, if reproduced, would make obesity the single most important risk factor for stillbirth in the general population. When considering the much smaller subset of women who are morbidly obese, the PAR for this group is 5.7% overall and as high as 8% at 40-42 weeks' gestation. As a comparison, the reported PARs for stillbirth for pregestational hypertension and diabetes mellitus, which are both classically considered “high-risk” conditions in the United States, are 8.0% and 3.9%, respectively.²²

Recently, Mandujano et al²³ described a method of calculating the risk of stillbirth for all undelivered pregnancies for a given gestational age, that is, for fetuses remaining at risk. We believe this is the best method for studying stillbirth, because the results from the given formula allows for direct comparison with NDR if all undelivered patients were to be induced at the gestational age in question. Using this method, we found a gradual increase in fetuses who are at risk for stillbirth after 41 weeks' gestation for normal-weight, overweight, and class I obese women; a sharp increase at 41 weeks' gestation for class III obese women, and a sharp increase at 39 weeks' gestation for women in the group with

TABLE 3
Adjusted hazard ratio^{a,b} by gestation period

| Obesity class | Overall adjusted hazard ratio (n = 2,864,165) | | Weeks' gestation, adjusted hazard ratio | | | | | | | |
|----------------------------|---|--------------|---|-----------|---------------------|-----------|-----------------------|-----------|---------------------|------------|
| | 95% CI | hazard ratio | 30-33 (n = 38,899) | 95% CI | 34-36 (n = 186,113) | 95% CI | 37-39 (n = 1,838,880) | 95% CI | 40-42 (n = 774,311) | 95% CI |
| Overweight | 1.29-1.43 | 1.36 | 1.25 | 1.09-1.44 | 1.30 | 1.12-1.50 | 1.35 | 1.19-1.55 | 1.33 | 1.02-1.73 |
| Class I ^c | 1.62-1.83 | 1.71 | 1.39 | 1.17-1.66 | 1.60 | 1.34-1.89 | 1.93 | 1.65-2.25 | 2.30 | 1.73-3.07 |
| Class II ^d | 1.89-2.21 | 2.04 | 1.28 | 1.03-1.60 | 1.64 | 1.31-2.06 | 2.48 | 2.04-3.02 | 2.37 | 1.59-3.53 |
| Class III ^e | 2.28-2.74 | 2.50 | 1.41 | 1.09-1.84 | 1.78 | 1.35-2.36 | 3.20 | 2.57-3.98 | 3.30 | 2.07-5.27 |
| BMI, ≥50 kg/m ² | 2.54-3.81 | 3.11 | 1.69 | 0.93-3.09 | 1.61 | 0.85-3.04 | 2.95 | 1.71-5.09 | 8.91 | 4.08-19.47 |

BMI, body mass index; CI, confidence interval.

^a Hazard ratio calculated with Cox proportional hazard regression analysis; baseline comparison group: normal weight; ^b Results adjusted for maternal age, primiparity, education, no prenatal care, race/ethnicity, smoking, chronic hypertension and pregestational diabetes mellitus; ^c BMI, 30.0-34.9 kg/m²; ^d BMI, 35.0-39.9 kg/m²; ^e BMI, ≥40 kg/m².

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BMI ≥50 kg/m². When we compared these results for each obesity class to the NDR reported by Mandujano et al, using data from the National Center for Health Statistics, we found that fetuses who are at risk for stillbirth crosses NDR earlier as BMI increases. The gestational age at which fetuses who are at risk for stillbirth exceeds NDR is 41 weeks for normal weight and overweight women, 38 weeks for class I obese women, 37 weeks for class II and III obese women, and 36 weeks for women with BMI >50 kg/m². These findings point to the high risk nature of obese pregnancies. They also support the current widespread practice of delivering most pregnancies by 41 rather than 42 weeks' gestation among our lower weight classes; perinatal deaths began to increase at 41 weeks.

We analyzed a sizable cohort of >2.8 million pregnancies with >9000 stillbirths. However, we acknowledge the limitations to using this method. In combining 2 databases, we are limited in the scope of our analysis to variables that are common to both datasets. Additionally, differences in variable definition and coding meant we had to convert some variables from 1 state to match the other. These 2 states were similar in the type of information that was collected, and potential errors in converting between multiple states' datasets were avoided. All large population databases can be affected by coding errors, missing data, and data entry errors. We limited the effects these errors may have on the analysis by excluding cases where missing or grossly inaccurate information was apparent. However, in doing so, we excluded 30% of stillbirths from analysis. This group had a larger proportion of black, multiparous women with lower education level, which are all risk factors that are associated with obesity among the cohort that was analyzed. Although it is unclear what effects this group may have on our results, we speculate that their exclusion leads to an underestimated risk of stillbirth that is associated with obesity. Because data from only 2 regions were used, we may incorporate regional characteristics that cannot be generalized to other populations. However, the 2 states that were selected are

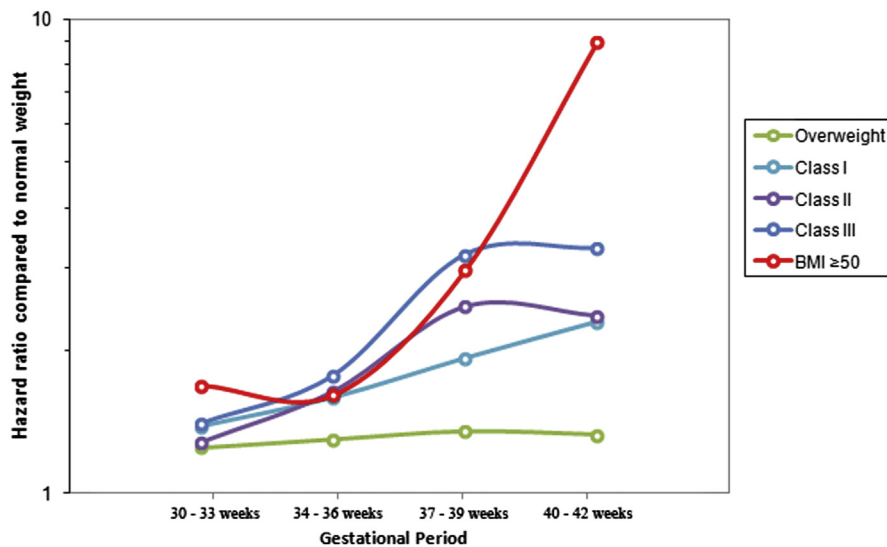
remote geographically from each other, and their population characteristics (eg, ethnic breakdown) are different, which should minimize this concern.

As part of the analysis, we excluded births that were complicated by birth defects from the databases. Many of the birth defects are either incompatible with life or associated with undiagnosed genetic conditions that increase risk for stillbirth. This is evident in this database in which 9% of stillbirths were noted to have ≥ 1 birth defects, whereas only 0.25% of the live births were noted to have any birth defects. The sensitivity of the databases that were analyzed for accurate recording of birth defects is unclear. However, the rates of specific birth defects that were excluded are similar compared with the national rates reported by the Center for Disease Control from 2004-2006.²⁴ We acknowledge that the gestational age for a reported stillbirth may not reflect accurately the timing of death, that is, the date of birth was recorded, but not the date of death. Delay from the actual time of stillbirth to time at which stillbirth is diagnosed will likely shift the results toward earlier gestation by an undeterminable length. However, the difference seems to be negligible in term pregnancies, based on previously published reports.^{25,26} Finally, it has been our experience and reported by others²⁷ that self-reported maternal prepregnancy weight commonly is underestimated. If anything, this would likely underestimate the differences between outcomes that were analyzed by weight class.

The strength of our study lies in the consistency of our findings with the use of various methods of statistical analysis. We are able to demonstrate the risk of stillbirth in our study population by calculating the fetuses who were at risk for stillbirth. Additionally, expressing stillbirth risk (based on BMI) based on the proportional hazards regression model accounts for heterogeneity in stillbirth risk across gestational age at delivery. This approach also provides a way to estimate adjusted HR based on the fetuses who are at risk approach.²⁸ The 2 analytical approaches yielded similar results in terms of the effect of obesity on

FIGURE 2

Risk of stillbirth by gestational period



The change in hazard ratio trend for each body mass index (BMI) class defined as the gestational period increases.

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stillbirth. Moreover, the large sample size in our study permitted us to estimate stillbirth risks in the extremely obese women and to make adjustment for a variety of confounders that previous studies have been unable to accomplish.

Our study provides further support for the concept that maternal obesity is associated with risk for fetuses and mothers. Although the findings as reported here are significant, especially for the most obese women for whom the risk for stillbirth is 6-fold higher at 39 weeks' gestation and 13 times higher at 41 weeks' gestation, these magnitude of the risk actually may be underestimated; this particular group has significantly higher comorbidities that, by themselves, would warrant frequent fetal testing and a tendency toward earlier delivery. As noted earlier, the rate of stillbirth for ongoing pregnancies outstrips the rate of neonatal death as early as 36 weeks' gestation for women whose BMI is ≥ 50 kg/m² and at 37 weeks' gestation for obese class II and III women. It is unclear, of course, whether delivery at this early a gestational age is optimal, given the increased neonatal morbidities that are associated

with early-term birth. At a minimum, based on the rapid rise in the rate of stillbirth for the most obese women (BMI, ≥ 40 kg/m² and particularly ≥ 50 kg/m²) after 39 weeks' gestation, we believe that any marginal improvement in maternal and neonatal morbidities are unlikely to justify prolonging pregnancy much beyond this point.

The mechanism that underlies the observed association between obesity and stillbirth remains elusive and likely to be multifactorial. Obese women are more likely to experience gestational hypertensive disorders and gestational diabetes mellitus, which are all risk factors for stillbirth. Some investigators have suggested that increased apneic-hypoxic events among obese women plays an important role.²⁹ Additionally, we propose that the pattern of stillbirth reported here (a sharp increase in the late term period) may be explained by the earlier development of uteroplacental insufficiency among obese women compared with normal weight women. This may be attributed partly to the increased growth velocity of fetuses among obese women, which is evident

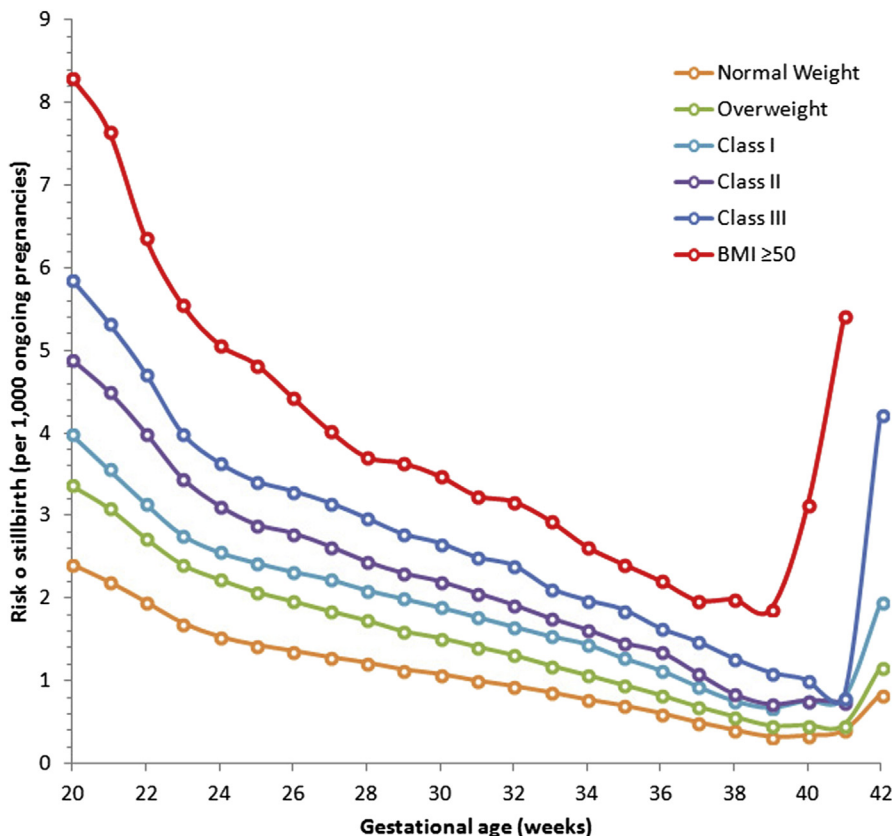
TABLE 4
Population attributable risk^{a,b}

| Obesity class | Overall | 95% CI | Weeks' gestation | | | | | | | |
|--|---------|-------------|------------------|------------|-------|---------------|-------|-------------|-------|-------------|
| | | | 30-33 | 95% CI | 34-36 | 95% CI | 37-39 | 95% CI | 40-42 | 95% CI |
| Overweight | 8.55 | 7.12–10.20 | 6.02 | 2.16–10.14 | 6.82 | 2.70–11.15 | 8.45 | 4.61–12.51 | 7.95 | 0.00–15.48 |
| Class I ^c | 8.48 | 7.37–9.67 | 5.12 | 2.16–8.38 | 7.61 | 4.57–10.94 | 10.96 | 7.92–14.20 | 13.88 | 8.24–20.30 |
| Class II ^d | 5.48 | 4.86–6.51 | 1.89 | 0.14–3.96 | 4.07 | 2.01–6.56 | 8.02 | 5.74–10.63 | 6.47 | 2.88–11.29 |
| Class III ^e | 4.73 | 4.06–5.46 | 1.76 | 0.31–3.59 | 3.04 | 1.34–5.21 | 4.43 | 3.20–5.92 | 5.78 | 2.77–10.23 |
| BMI, ≥ 50 kg/m ² | 0.92 | 0.67–1.21 | 0.02 | 0.00–0.07 | 0.39 | –0.10 to 1.29 | 0.88 | 0.32–1.82 | 2.24 | 0.89–5.08 |
| All obesity (BMI, ≥ 30 kg/m ²) | 19.61 | 16.96–22.85 | 8.79 | 2.61–16.00 | 15.11 | 7.83–24.00 | 24.29 | 17.19–32.56 | 28.38 | 14.78–46.90 |
| Morbid obesity (BMI, ≥ 40 kg/m ²) | 5.65 | 4.73–6.67 | 1.78 | 0.31–3.66 | 3.43 | 1.25–6.50 | 5.31 | 3.52–7.74 | 8.02 | 3.65–15.31 |

BMI, body mass index; CI, confidence interval.

^a Population-attributable risk based on adjusted hazard ratio; ^b Results adjusted for maternal age, primiparity, education, no prenatal care, race/ethnicity, smoking, chronic hypertension and pregestational diabetes mellitus; ^c BMI, 30.0–34.9 kg/m²; ^d BMI, 35.0–39.9 kg/m²; ^e BMI, ≥ 40 kg/m².

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FIGURE 3
Risk of stillbirth for remaining pregnancies

Week-by-week comparison of the risks of stillbirth for undelivered pregnancies for each body mass index (BMI) class defined.

Yao. Obesity and the risk of stillbirth. *Am J Obstet Gynecol* 2014.

by their risk for the development of macrosomia³⁰ and evidence for placental inflammation and decreased placental growth.^{31,32}

To date, we have no data about the utility of fetal surveillance (eg, cardiotocography, nonstress testing, biophysical profile assessment) in reducing the risk of stillbirth in obese women; however, extrapolating from other groups at increased risk of stillbirth, it may be reasonable to undertake these measures. Certainly, the obese abdominal wall may make monitoring more difficult than in other cases, and of course, the positive predictive value of antenatal testing is limited. Additionally, because of the limitations of these databases, we are unable to determine the indications for delivery such as for spontaneous labor or medically indicated delivery. Answering this question may help in determining the effectiveness of current fetal surveillance regimens and interventions in preventing stillbirth. We believe that future efforts should be directed toward the identification of the optimal labor induction time for each obesity class separately, the determination of the utility of fetal surveillance among obese women, and the confirmation of the pathophysiologic evidence behind the association between obesity and stillbirth. ■

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