Simulated Estimates of Pre-Pregnancy and Gestational Diabetes Mellitus in the US: 1980 to 2008

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Abstract

**Purpose:** To simulate national estimates of prepregnancy and gestational diabetes mellitus (GDM) in non-Hispanic white (NHW) and non-Hispanic black (NHB) women.

**Methods:** Prepregnancy diabetes and GDM were estimated as a function of age, race/ethnicity, and body mass index (BMI) using South Carolina live singleton births from 2004–2008. Diabetes risk was applied to a simulated population. Age, natality and BMI were assigned to women according to race- and age-specific US Census, Natality and National Health and Nutrition Examination Surveys (NHANES) data, respectively.

**Results:** From 1980–2008, estimated GDM prevalence increased from 4.11% to 6.80% [2.68% (95% CI 2.58%–2.78%)] and from 3.96% to 6.43% [2.47% (95% CI 2.39%–2.55%)] in NHW and NHB women, respectively. In NHB women prepregnancy diabetes prevalence increased 0.90% (95% CI 0.85%–0.95%) from 0.95% in 1980 to 1.85% in 2008. In NHB women from 1980 through 2008 estimated prepregnancy diabetes prevalence increased 1.51% (95% CI 1.44%–1.57%), from 1.66% to 3.16%.

**Conclusions:** Racial disparities in diabetes prevalence during pregnancy appear to stem from a higher prevalence of prepregnancy diabetes, but not GDM, in NHB than NHW.

Introduction

Several factors influence diabetes prevalence during pregnancy and thus, make it difficult to compare prevalence over time or across populations. Namely, changes in diagnostic criteria as well as screening policies concerning gestational diabetes mellitus (GDM). At the 4th International Workshop conference on GDM in 1997, a critical change in the GDM diagnostic criteria occurred when it was largely agreed that the Carter & Coustan criteria replace the National Diabetes Data Group criteria, significantly lowering the accepted cut-points, thus increasing the prevalence of GDM [1]. Moreover, as awareness of GDM has increased screening has also increased, further increasing the prevalence of diagnosted GDM. Finally, because GDM encompasses undiagnosed type 2 diabetes prior to pregnancy, the definition, screening strategies, and awareness of type 2 diabetes ultimately influences the observed prevalence of GDM. The diagnostic criteria and screening practices for diabetes changed in 1997 when the threshold for a fasting glucose level diagnostic of diabetes was lowered from 140 mg/dL to 126 mg/dL (7.0 to 7.8 mmol per L) [2,3].

Increased maternal age and prepregnancy BMI are both strong risk factors for GDM and contributing factors to increased prevalence rates. However, using standard methodology it is not feasible to examine the impact of these factors on GDM prevalence without systematically following a large cohort of women. As pregnancy is a rare event, in countries without national registries, such as the US, it is not feasible to routinely obtain a nationally representative sample of pregnant women and complete a clinical examination during pregnancy. Tracking members through their electronic medical records as has been done in the Kaiser managed health care organization comes the closest to a comprehensive cohort [4], but remains subject to secular trends in the diagnosis of GDM and type 2 diabetes (i.e., changes in the diagnostic criteria as well as changes in screening strategies and awareness of type 2 diabetes in women of childbearing age).

Estimates of recognized gestational diabetes during pregnancy from prior studies range from 2 to 10% of the pregnancies in the US, with higher estimates for racial and ethnic minority groups than for non-Hispanic whites (NHWs) [5]. Once diagnosed with GDM, a woman has a high chance of developing type 2 diabetes, with cumulative incidence estimates of 15–50% in the decades following delivery [6]. A recent meta-analysis reports a 7-fold increase in risk of developing type 2 diabetes in women with prior GDM relative to women without diabetes during pregnancy [7]. Other studies indicate that women with GDM also have increased...
cardio-metabolic and cardiovascular disease risk[7–9]. Moreover, the ‘early origin of disease’ hypothesis proposes that gestational programming may critically influence adult health and disease [10]. Exposure to maternal diabetes early in pregnancy is associated with high birthweight, macrosomia, increased child- and adult obesity and increased risk of type 2 diabetes[12–15]. We postulate that if the diabetic intrauterine environment substantially contributes to the obesity and diabetes epidemics, their prevalence will continue to increase perpetuating health disparities between racial and ethnic groups, as populations with high prevalence will continue to be disproportionately exposed.

Previous studies have focused on projections of diabetes prevalence in the general population, and have not included GDM. Projections of diabetes prevalence in the US population have been completed through 2030 [19] and 2050 [20] and also globally through 2030 [21]. In contrast, our objective was to estimate the prevalence of prepregnancy diabetes and GDM in the US from 1980 through 2008 in NHW and NHB women 15 to 44-years-old. Additionally, we investigated the extent that the obesity epidemic and maternal age at delivery have influenced trends in diabetes during pregnancy.

Methods

A mixed-methods approach was used with a statistical model used to inform the parameters of a simulation model. Figure 1 provides a conceptual representation of the methodology. In a logistic regression model, we estimate the risk of diabetes during pregnancy (prepregnancy and GDM) based on age, race/ethnicity, and body mass index (BMI). Then, we simulated a cohort with US population level characteristics (race/ethnicity, age, race- and age-specific BMI, and natality rates) and apply risk of diabetes based on regression estimates.

Data

Live singleton births of South Carolina (SC) resident mothers between January 2004 and December 2008 were used to estimate the risk of diabetes during pregnancy. The mothers included in the study were 15 to 44-year-old NHW (n = 151,362) or NHB (n = 91,737) women. Birth certificate information was obtained from the SC Department of Health and Environmental Control and linked by the SC Office of Research and Statistics (ORS) to prenatal hospital discharge records to obtain maternal inpatient procedure and diagnostic codes pertaining to delivery. Additionally, outpatient diagnostic codes were available for the prenatal period if care was received through Medicaid or the State Health Plan. The algorithm linking the databases used personal identifying information and was developed by ORS.

US population level maternal diabetes prevalence projections were made using National Health and Nutrition Examination Surveys (NHANES) data on BMI and natality produced by the National Center for Health Statistics and age distribution data from the US Census. We used NHANES II (1976–1980), III (1988–1994), and continuous NHANES cycles 1999–2000, 2001–2002, 2005–2006, and 2007–2008 data [12]. Age- and race/ethnicity-specific natality data [22] and race-specific age distribution of NHW and NHB women ages 15–44[23–25] were obtained for 1980, 1990, 2000 and 2008. Table 1 provides extracted data.

Ethics Statement

The Institutional Review Board of the Medical University of South Carolina approved the study as exempt research (HR Number 19410, August 25, 2009 to August 25, 2014) and waived the need for informed consent given the use of routinely collected de-identified patient data for this analysis.

Statistical Model Variable Definition

Diabetes during pregnancy was defined by either GDM or prepregnancy diabetes reported on the birth certificate, or if it was coded as such on the inpatient hospital discharge records or during the prenatal period. The prenatal period was defined by the date of delivery, gestational age of the infant at delivery, and included the year prior to conception in defining prepregnancy diabetes. For a diagnosis of diabetes during pregnancy based on the prenatal data alone two or more ICD-9-CM diagnostic codes indicative of diabetes were required in the medical record [14,26]. Primary and secondary inpatient hospital and prenatal ICD-9-CM diagnosis codes used to define diabetes included those for prepregnancy diabetes (i.e., 25000–25092), and GDM (i.e., 64801–64802, 64881–64882). Further classification into having prepregnancy diabetes or GDM was based on evidence of prepregnancy diabetes from any source; hence, the prepregnancy diabetes classification overruled. Maternal prepregnancy BMI (in kg/m²) was calculated based on maternal height and self-reported pre-pregnancy weight which are reported on the birth certificate. Self-reported weight and height are systematically under-reported [27,28] and prepregnancy weight is inherently self-reported, therefore, it was assumed that BMI was under-reported by 5%; a sensitivity analysis compares results at 0% and 10% under-report.

![Figure 1. High level overview of methodology]( doi:10.1371/journal.pone.0073437.g001)
The goal of our statistical analysis was to develop a model for the risk of diabetes during pregnancy, due to either prepregnancy diabetes or GDM. We did this with two (nested) logistic regression models which use the data from live singleton births in SC to estimate the risk of diabetes by type (GDM or prepregnancy diabetes) as a function of age (15–44-years-old), race/ethnicity, and BMI (rounded to the nearest whole number). The first (top models which use the data from live singleton births in SC to estimate the risk of diabetes by type (GDM or prepregnancy diabetes) as a function of age (15–44-years-old), race/ethnicity, and BMI (rounded to the nearest whole number). The first (top
level) model estimated the aggregate risk of diabetes during pregnancy (DM), defined as GDM or prepregnancy diabetes. The second model (nested level) used only the subset of data which included women with diabetes in order to estimate the likelihood that the woman had diabetes prior to pregnancy given that she had diabetes during pregnancy. From these results we extract the risk of GDM. Both regression models use the same explanatory variables as described in Equation 1, \( \pi_i \) is the intercept, \( \beta_1, \beta_2 \) are the coefficients corresponding to \( Race, BMI, BMI^2, Age, Age^2 \), and the random intercept \( \epsilon_i \) terms allows for differences in individual response when predictors have the same value. Both models predict the probability \( (\pi_i) \) that the individual has diabetes, during pregnancy (DM) in the case of the top level model and prepregnancy diabetes given DM in the case of the nested level. The equation describes the relative effect of each predictor on the woman’s risk of disease (DM, prepregnancy diabetes given DM). The quadratic terms in BMI and Age are included to capture the non-linear trend we anticipate in the model for these variables. The analysis was performed in Statistical Analysis System (SAS) 9.2 using GLIMMIX procedure, which allows random effects.

\[
\log(\pi_i) = \ln\left(\frac{\pi_i}{1-\pi_i}\right) = \alpha + \beta_1 \times Race + \beta_2 \times BMI + \beta_3 \times BMI^2 + \beta_4 \times Age + \beta_5 \times Age^2 + \epsilon_i 
\]

(1)

Model diagnostics and goodness of fit tests were performed using residual plots and observed-predicted value plots.

**Simulation Model**

Our estimates of diabetes risk captured the mean response of an individual with a given set of characteristics. These results were then used to estimate the risk at a population level by assigning risk to simulated individuals. Simulation is an analytical tool used for evaluation of complex stochastic systems and for consideration of probable changes in those systems due to different sources of variation. In recent years, simulation has emerged as a powerful tool for health and economic evaluation [29,30], and has been used to estimate the cost-effectiveness of treatment strategies for type 2 diabetes[31–33] and for screening practices for GDM [34].

We developed a simulation model of individuals in a population. We applied the predicted risk of diabetes during pregnancy to simulated individuals to estimate maternal diabetes prevalence at the population-level. First, 100,000 NHW and 100,000 NHB women were created whose ages conformed to the US Census distribution of age between 15–44-years-old. Second, race- and age-specific maternal BMI was also individually assigned based on estimates from NHANES. All analyses of NHANES data were conducted using the complex survey-specific procedures in SAS to account for the clustered sampling design and over-sampling, and were adjusted for differential non-coverage and non-response across each NHANES cycle [12]. We tested the fit of the distribution of BMI and found that the lognormal and gamma distributions provided the best fit based on least mean squared error. We used the gamma distribution for BMI stratified by age, race and year; the shape and scale parameters of the gamma distribution were chosen such that the distribution’s mean and variance matched the mean and variance of the NHANES data for each year, race and age. Third, pregnancies were assigned to women according to race- and age-specific US natality data. Lastly, we simulated whether or not an individual developed diabetes. An individual’s risk of developing diabetes was based on age, race/ethnicity and BMI. Based on the two logistic regression models, women were first at risk of any type of diabetes during pregnancy (DM), then a portion of the women with diabetes were assigned prepregnancy diabetes. Simulation allows us to obtain different results for individuals with the same attributes and resulting risk level. Specifically, an individual’s risk of diabetes during pregnancy \( p_i \) is determined by the logistic regression model (eq. 1), then we draw a random number between 0 and 1. If that random number is less than \( p_i \) then the individual is said to have diabetes, if the random number is greater than \( p_i \) then they are not diabetic. For example, if \( p_i = 0.25 \) then any random number drawn between 0 and 0.25 will result is an individual being assigned diabetes, since random numbers are generated uniformly between 0 and 1, each individual will develop diabetes with probability \( p_i \), as is our goal. While the point estimate of the estimated risk \( p_i \) is the same as the point estimate of the predicted risk, the standard error for the estimated risk (which accounts for uncertainty in the regression) is different than the standard error of the predicted risk (which accounts for both uncertainty in the regression and in the individual observation). Based on the sufficiently large sample size, the prediction standard error was approximated as the standard error for each estimate. Thus, the predicted values (and standard error) for every possible combination of model parameters were outputs of the regression models and are used to define the normal distribution of the risk of a woman developing diabetes used in the simulation.

In summary, variability in the model comes from two sources. First, race- and age-specific BMI is drawn from a distribution based on NHANES data. Second, the prediction error of the risk of diabetes (DM and GDM) estimated in the logistic regression model is normally distributed such that individuals with the same characteristics experience a different risk of diabetes during pregnancy. We used the same random number stream [35] for both NHB and NHW women when assigning age and BMI in order to remove variance attributable to different individual characteristics. We report diabetes prevalence in 5-year age groups between 15 and 44-years-old stratified by race/ethnicity for 1980, 1990, 2000, and 2008. The model was developed using Arena 13.5 and validated using the sample of SC women with known age, race, BMI, and diabetes statuses. The 95% CIs of the simulation estimates for diabetes prevalence (i.e., any diabetes, GDM, prepregnancy diabetes) covered the actual prevalence of the sample for both NHB and NHW women. Table 2 provides descriptive statistics of the SC sample. Simulated results used 40 replications; this was decided based on a desired half-width of <.2% for the overall prevalence estimates. See [36] for information on selecting number of replications. Rounding was done to the nearest decimal and results in CIs that appear to be of 0% width. Rounding may impact point estimates reported in results.

**Results**

The regression predictor estimates (and 95% confidence intervals) for diabetes and prepregnancy diabetes risk (given DM) are provided in Table 3. These are then used in the simulation model, as discussed in the methods section, to obtain our national estimates. Validation of our simulation approach is provided in Table 2B. This shows that the methodology of using our statistical model applied to a simulated population accurately predicts outcomes for that population. This is not a validation of the regression model itself, but rather of the approach.

From 1980 through 2008, in NHW the estimated prevalence of GDM increased 2.7% (95% CI 2.6%–2.8%) (Table 4). All prevalence estimates are reported to the single decimal point so
The estimated diabetes prevalence during pregnancy increased between 1980 and 2008 within each age group in NHW women. However, the estimated prevalence increased in younger NHB women, but leveled off between 2000 and 2008 in NHB women. The projected increase in diabetes prevalence during pregnancy from 1980–2008 was also evaluated (Figure 2, Scenario 1; 2008 prevalence given increased maternal age at birth without the obesity epidemic). The projections indicate that the prevalence of GDM in 2008 would have been 5.2% (95% CI 5.1%–5.2%) representing a significant increase over prevalence estimates in 1980 [4.1% (95% CI 4.0%–4.2%)]. The projections also indicate that the prevalence of prepregnancy diabetes in 2008 would have been 1.2% (95% CI 1.2%–1.3%) representing a significant increase over prevalence estimates in 1980 [1.0% (95% CI 0.9%–1.0%)]. Results were similar in NHB.

Similarly, the potential impact of increases in maternal BMI on diabetes prevalence during pregnancy from 1980–2008 was also evaluated (Figure 2, Scenario 2; 2008 prevalence given increased maternal BMI without increased maternal age at delivery). The projections indicate that the prevalence of GDM in 2008 would have been 5.5% (95% CI 5.4%–5.6%) which represents a significant increase over prevalence estimates in 1980 [4.1% (95% CI 4.0%–4.2%)]. The projections also indicate that the prevalence of prepregnancy diabetes in 2008 would have been 1.5% (95% CI 1.4%–1.5%) which represents a significant increase over prevalence estimates in 1980 [1.0% (95% CI 0.9%–1.0%)]. Results were similar in NHB.

Finally, we completed a sensitivity analysis to examine the impact of under-reporting prepregnancy weight on the birth certificate (see Table 4) at 0%, 5% (base case), and 10% BMI under-report levels. Diabetes prevalence estimates (total and by type) in NH and NHB women were statistically higher when BMI is assumed to be reported correctly and statistically lower when BMI is assumed to be under-reported by 10% (Table 4).

### Discussion

This study examined the impact of changes in maternal age and prepregnancy BMI on the prevalence of GDM and prepregnancy diabetes over time at the national level in NHW and NHB women. From 1980–2008, simulation estimates of diabetes prevalence in pregnant NHW and NHB women increased, with higher increases over time in diabetes prevalence in NHB than NHW women. Interestingly, at each time point the higher diabetes prevalence during pregnancy in NHBs resulted solely from higher levels of prepregnancy diabetes with GDM prevalence levels actually being lower in NHB than NHW women subsequent to 1980.

Our national prevalence estimates for prepregnancy diabetes and GDM follow the same pattern, but are slightly higher than results from a study in Southern California that reports 2005 prevalence estimates for prepregnancy diabetes of 1.5% in NHW women, the increase in prevalence was highest in women 35–39 years-old (Table 4). For example, diabetes prevalence increased from 1.7% (95% CI 1.6%–1.7%) to 3.2% (95% CI 3.1%–3.2%). Prepregnancy diabetes prevalence estimates were higher in NHB than NHW women in 1980 through 2008, with differences increasing over time (see Table 4). Combining these changes resulted in an overall increase in the estimated diabetes prevalence during pregnancy of 3.6% (95% CI 3.5%–3.7%) in NHW and 4.0% (95% CI 3.9%–4.1%) in NHB women.

The estimated diabetes prevalence during pregnancy increased between 1980 and 2008 within each age group in NHW women. However, the estimated prevalence increased in younger NHB women, but leveled off between 2000 and 2008 in NHB women between 30–34 and 40–44 years-old (Table 4). For example, prevalence estimate for women ages 40–44 in 2008 was 18.6% (95% CI 17.3%–19.8) in NHW and 21.3% (95% CI 20.0%–22.5%) in NHB. In NHB women the prevalence increase was highest in women 40–44 (3.33%, 95% CI 1.3%–5.4%) and lowest in those ages 15–19 (0.6%, 95% CI 0.4%–0.9%). For NHW women, the increase in prevalence was highest in women 35–39 (3.8%, 95% CI 3.1%–4.5%) and lowest in those ages 15–19 (1.5%, 95% CI 1.3%–1.6%).

### Table 2. SC population characteristics and simulation validation.

| A. Characteristics of pregnant women in SC | B. Simulation validation |
|------------------------------------------|--------------------------|
| Mean age | Mean BMI (kg/m²) | % of pregnant women with diabetes |
| NHW | 27.1 | 27.5 | Actual | Simulated (95% CI) |
| NHB | 24.7 | 30.4 | | | |
| Prepregnancy DM | | | | | |
| NHW | 1.7 | 1.7 (1.7, 1.8) | | | |
| NHB | 2.9 | 2.9 (2.9, 3.0) | | | |
| GDM | | | | | |
| NHW | 6.3 | 6.4 (6.3, 6.4) | | | |
| NHB | 6.0 | 6.1 (6.0, 6.1) | | | |

### Table 3. Logistic regression equation predictor estimates.

| Predictor | Diabetes | Prepregnancy Diabetes |
|-----------|----------|-----------------------|
| Intercept | -8.5440 | -1.2150 |
| Race, NHB | 0.0500 | 0.4614 |
| BMI, kg/m² | 0.1552 | 0.0407 |
| BMI², kg/m² | -0.0013 | -0.0002 |
| Age | 0.1230 | -0.0753 |
| Age² | -0.0009 | 0.0011 |

Results assume BMI is underreported by 5%.

The potential impact of increases in maternal age at delivery on diabetes prevalence during pregnancy from 1980–2008 was evaluated (Figure 2). This study examined the impact of changes in maternal age and prepregnancy BMI on the prevalence of GDM and prepregnancy diabetes over time at the national level in NHW and NHB women. From 1980–2008, simulation estimates of diabetes prevalence in pregnant NHW and NHB women increased, with higher increases over time in diabetes prevalence in NHB than NHW women. Interestingly, at each time point the higher diabetes prevalence during pregnancy in NHBs resulted solely from higher levels of prepregnancy diabetes with GDM prevalence levels actually being lower in NHB than NHW women subsequent to 1980.
and 2.6% in NHB, and prevalence estimates for GDM of 5.3% in NHW and 5.0% in NHB [4]. In contrast, our national prevalence estimates are much higher, but follow similar increasing trends as a national study based solely on hospital discharge data that reported diabetes prevalence during pregnancy (i.e., prepregnancy and GDM combined) increased from 3.49% in 1994 to 5.47% in 2004 [37]. Similarly, a study based on National Hospital Discharge Survey’s reported the prevalence of GDM increased from 2.0% to 3.6% in white women and from 1.5% to 4.1% in black women from 1989 to 2004 [38].

Table 4. US population simulation estimates of diabetes prevalence (95% CI) during pregnancy in non-Hispanic white and non-Hispanic black women ages 15–44.

|                          | non-Hispanic white | non-Hispanic black |
|--------------------------|--------------------|--------------------|
|                          | 1980   | 1990   | 2000   | 2008   | 1980   | 1990   | 2000   | 2008   |
| **MAIN ANALYSIS**        |        |        |        |        |        |        |        |        |
| 5% BMI under-report      |        |        |        |        |        |        |        |        |
| Diabetes                 |        |        |        |        |        |        |        |        |
| Total                    | 5.1(5.0, 5.2) | 6.5(6.4, 6.6) | 8.1(8.0, 8.2) | 8.7(8.5, 8.8) | 5.6(5.6, 5.7) | 7.1(7.1, 7.2) | 8.9(8.8, 9.0) | 9.6(9.5, 9.7) |
| Ages 15–19                | 2.2(2.0, 2.3) | 2.6(2.4, 2.7) | 2.8(2.6, 3.1) | 2.8(2.5, 3.0) | 2.6(2.5, 2.7) | 3.2(3.1, 3.3) | 3.7(3.6, 3.8) | 4.1(3.9, 4.2) |
| Ages 20–24                | 3.4(3.3, 3.6) | 3.8(3.7, 4.0) | 4.9(4.7, 5.1) | 5.0(4.8, 5.2) | 4.2(4.1, 4.3) | 5.0(4.9, 5.1) | 6.3(6.1, 6.4) | 6.7(6.5, 7.0) |
| Ages 25–29                | 5.5(5.3, 5.7) | 5.9(5.7, 6.1) | 7.1(6.9, 7.3) | 7.8(7.6, 8.0) | 7.0(6.9, 7.2) | 7.9(7.8, 8.1) | 9.8(9.6, 10.0) | 10.0(9.8, 10.2) |
| Ages 30–34                | 8.1(7.9, 8.4) | 9.1(8.8, 9.3) | 10.0(9.8, 10.2) | 10.9(10.7, 11.1) | 10.7(10.5, 11.0) | 12.4(12.1, 12.7) | 14.2(13.9, 14.5) | 14.3(14.0, 14.6) |
| Ages 35–39                | 11.0(10.4, 11.5) | 13.0(12.5, 13.4) | 13.8(13.5, 14.1) | 14.1(13.6, 14.6) | 14.7(14.1, 15.3) | 16.1(15.6, 16.6) | 16.7(16.2, 17.3) | 18.5(17.9, 19.1) |
| Ages 40–44                | 15.2(13.2, 17.2) | 14.9(13.5, 16.3) | 16.4(15.2, 17.6) | 18.6(17.3, 19.8) | 18.4(16.6, 20.2) | 20.6(19.1, 22.1) | 21.4(21.2, 23.1) | 21.3(20.0, 22.5) |
| Prepregnancy diabetes     | 1.0(0.9, 1.0) | 1.3(1.3, 1.3) | 1.7(1.6, 1.7) | 1.9(1.8, 1.9) | 1.7(1.6, 1.7) | 2.2(2.1, 2.2) | 2.9(2.8, 3.0) | 3.2(3.1, 3.2) |
| GDM                      | 4.1(4.0, 4.2) | 5.2(5.2, 5.3) | 6.4(6.3, 6.5) | 6.8(6.7, 6.9) | 4.0(3.9, 4.0) | 4.9(4.9, 5.0) | 6.0(6.0, 6.1) | 6.4(6.3, 6.5) |
| **SENSITIVITY ANALYSIS**  |        |        |        |        |        |        |        |        |
| 0% BMI under-report      |        |        |        |        |        |        |        |        |
| Diabetes                 | 5.6(5.5, 5.7) | 7.2(7.1, 7.3) | 8.9(8.8, 9.0) | 9.5(9.4, 9.6) | 6.2(6.1, 6.3) | 7.8(7.7, 7.9) | 9.7(9.6, 9.8) | 10.4(10.3, 10.5) |
| Prepregnancy DM          | 1.1(1.1, 1.1) | 1.5(1.5, 1.5) | 1.9(1.8, 2.0) | 2.1(2.0, 2.2) | 1.9(1.9, 1.9) | 2.5(2.4, 2.6) | 3.2(3.1, 3.3) | 3.5(3.4, 3.6) |
| GDM                      | 4.5(4.4, 4.6) | 5.7(5.6, 5.8) | 7.0(6.9, 7.1) | 7.5(7.4, 7.6) | 4.3(4.2, 4.4) | 5.3(5.2, 5.4) | 6.5(6.4, 6.6) | 6.9(6.8, 7.0) |
| 10% BMI under-report     |        |        |        |        |        |        |        |        |
| Diabetes                 | 4.6(4.5, 4.7) | 6.0(5.9, 6.1) | 7.4(7.3, 7.5) | 7.9(7.8, 8.0) | 5.1(5.0, 5.2) | 6.5(6.4, 6.6) | 8.1(8.0, 8.2) | 8.9(8.8, 9.0) |
| Prepregnancy DM          | 0.8(0.8, 0.8) | 1.1(1.1, 1.1) | 1.5(1.4, 1.6) | 1.6(1.6, 1.6) | 1.5(1.5, 1.5) | 2.0(2.0, 2.0) | 2.5(2.4, 2.6) | 2.9(2.8, 3.0) |
| GDM                      | 3.8(3.7, 3.9) | 4.8(4.7, 4.9) | 5.9(5.8, 6.0) | 6.3(6.2, 6.4) | 3.7(3.6, 3.8) | 4.5(4.4, 4.6) | 5.6(5.5, 5.7) | 6.0(5.9, 6.1) |

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however, our study is unable to address the impact of this change on the projected diabetes prevalence during pregnancy. A strength of our approach is that risk was assigned uniformly over time and varied only due to changes in the race/ethnicity-specific maternal age, BMI and natality structure of the population; hence, it was possible to examine the potential impact of each of these items on diabetes prevalence during pregnancy from 1980 through 2008. Furthermore we were able to examine trends over time without the effects of changes in definition, screening, or awareness. The results of this study indicate that increased maternal age and the obesity epidemic both contribute substantially to the increasing prevalence of GDM as well as prepregnancy diabetes. Racial disparities in diabetes prevalence during pregnancy appear to stem from a higher prevalence of prepregnancy diabetes in NHB than NHW women, with slightly lower prevalence estimates for GDM in NHB than NHW women. The increasing prevalence of prepregnancy diabetes is disconcerting given that diagnosis of diabetes at a younger age results in greater duration, co-morbidity burden and earlier mortality [45]. Exposure to maternal diabetes early in pregnancy is associated with birth defects, high birth weight, increased childhood and adult obesity and increased risk of type 2 diabetes later in pregnancy [12,13,15,18,46]. Interventions are required that increase the awareness and control of diabetes prior to pregnancy and prevent the development to type 2 diabetes following GDM.

Author Contributions
Conceived and designed the experiments: MEM OSR DMN MGG KJH. Performed the experiments: MEM OSR. Analyzed the data: MEM OSR DMN MGG KJH. Contributed reagents/materials/analysis tools: MEM MGG KJH. Wrote the paper: MEM OSR DMN MGG KJH. Obtained SC data: KJH. Developed simulation model: MEM OSR.

References

1. Metzger BE, Coustan DR (1998) Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. The Organizing Committee. Diabetes Care 21 Suppl 2: B161–167.
2. Alberti KG, Zimmet PZ (1998) Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 15: 539–553.
3. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (2003) Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 26 Suppl 1: S5–20.
4. Lawrence JM, Contreras R, Chen W, Sacks DA (2008) Trends in the prevalence of preexisting diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women, 1999–2005. Diabetes Care 31: 899–904.

5. Hunt KJ, Schuller KL (2007) The increasing prevalence of diabetes in pregnancy. Obstet Gynecol Clin North Am 34: 173–199, vii.
6. Kim C, Newton KM, Knopp RH (2002) Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care 25: 1862–1868.
7. Bellamy L, Casas JP, Hingorani AD, Williams D (2009) Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 373: 1773–1779.
8. Fraser A, Nelson SM, Macdonald-Wallis C, Cherry I, Butler E, et al. (2012) Associations of Pregnancy Complications With Calculated Cardiovascular Disease Risk and Cardiovascular Risk Factors in Middle Age/Clinical Perspective. Circulation 125: 1367–1380.
9. Shah BR, Retnakaran R, Booth GL (2008) Increased Risk of Cardiovascular Disease in Young Women Following Gestational Diabetes Mellitus. Diabetes Care 31: 1668–1669.
10. Barker DJ (1995) Fetal origins of coronary heart disease. BMJ 311: 171–174.
11. Dunne F, Brydou P, Smith K, Gee H (2003) Pregnancy in women with Type 2 diabetes: 12 years outcome data 1990–2002. Diabet Med 20: 734–739.
12. Dahleka D, Hanson RL, Lindsay RS, Pettitt DJ, Imperatore G, et al. (2000) Intratime exposure to diabetes conveys risks for type 2 diabetes and obesity: a study of discordant sibships. Diabetes 49: 2208–2211.
13. Freinkel N (1980) Banting Lecture 1980. Of pregnancy and progeny. Diabetes 29: 1023–1035.
14. Hunt KJ, Marlow NM, Gebregziabher M, Eillerbe CN, Mauldin J, et al. (2012) Impact of maternal diabetes on birthweight is greater in non-Hispanic blacks than in non-Hispanic whites. Diabetologia 55: 971–980.
15. Pettitt DJ, Knowler WC. (1998) Long-term effects of the intrauterine environment, birth weight, and breast-feeding in Pima Indians. Diabetes Care 21 Suppl 2: B138–B141.
16. Pettitt DJ, Knowler WC, Baird HR, Bennett PH (1980) Gestational diabetes: infant and maternal complications of pregnancy in relation to third-trimester glucose tolerance in the Pima Indians. Diabetes Care 3: 458–464.
17. Pettitt DJ, Knowler WC, Bennett PH, Aleck KA, Baird HR. (1987) Obesity in offspring of diabetic Pima Indian women despite normal birth weight. Diabetes Care 10: 76–90.
18. Silverman BL, Rizzo T, Green OC, Cho NH, Winter RJ, et al. (1991) Long-term prospective evaluation of offspring of diabetic mothers. Diabetes 40 Suppl 2: 121–125.
19. Mainous A, Baker R, Koopman R, Saenz S, Diaz V, et al. (2007) Impact of the population at risk of diabetes on projections of diabetes burden in the United States: an epidemic on the way. Diabetologia 50: 934–940.
20. Boyle JP, Honeycutt AA, Narayan KMV, Hoerger TJ, Geiss LS, et al. (2001) Detailed Data Files. US Census Bureau (1980) 1980 Census of Population and Housing County Characteristics. pp. Table 4: 1950–2000.
21. King H, Aubert RE, Herman WH (1998) Global Burden of Diabetes, 1995–2025: Prevalence, numerical estimates, and projections. Diabetes Care 21: 1414–1431.
22. National Center for Health Statistics (2012) Health, United States, 2011: With Special Feature on Socioeconomic Status and Health. In: Statistics NCfH, editor. Hyattsville, Maryland. pp. Table 3. Crude birth rates, fertility rates, and birth rates, by age, race, and Hispanic origin of mother: United States, selected years 1950–2008.
23. US Census Bureau (1980) 1980 Census of Population and Housing County Population by Age, Sex, Race, and Spanish Origin. pp. Table IV.
24. US Census Bureau (1992) 1990 Census of Population: General Population Characteristics. pp. Table 13: Single Years of Age by Sex, Race, and Hispanic Origin: 1990.
25. US Census Bureau (2004) Population Projections: U.S. Interim Projections by Age, Sex, Race, and Hispanic Origin: 2000–2050 In: Division P, editor. pp. Detailed Data Files.
26. Miller DR, Safford MM, Pogach LM (2004) Who has diabetes? Best estimates of diabetes prevalence in the Department of Veterans Affairs based on computerized patient data. Diabetes Care 27 Suppl 2: B10–B11.
27. Engstrom JL, Paterson SA, Doherty A, Trabulsi M, Speer KL (2003) Accuracy of self-reported height and weight in women: an integrative review of the literature. J Midwifery Womens Health 48: 338–345.
28. Ezzati M, Martin H, Skjold S, Vander Hoorn S, Murray CJ (2006) Trend in national and state-level obesity in the USA after correction for self-report bias: analysis of health surveys. J R Soc Med 99: 250–257.
29. Caro J (2005) Pharmacoeconomic analyses using discrete event simulation. Pharmacoeconomics 23: 323–332.
30. Caro J, Moller J, Getson D (2010) Discrete event simulation: the preferred technique for health economic evaluations? Value Health 13: 1056–1060.
31. Brandle M, Assoulay M, Geizer RA (2011) Cost-effectiveness of insulin glargine versus NPH insulin for the treatment of Type 2 diabetes mellitus, modeling the interaction between hypoglycemia and glyemic control in Switzerland. Int J Clin Pharmacol Ther 49: 217–230.
32. Erdhardt W, Bengenheim K, Duprat-Lomon I, McEwan P (2012) Cost effectiveness of saxagliptin and metformin versus sulfonfonylurea and metformin in the treatment of type 2 diabetes mellitus in Germany: a Cardiff diabetes model analysis. Clin Drug Investig 32: 189–202.
33. Pollock RF, Valentine WJ, Pilgaard T, Nishimura H (2011) The cost effectiveness of rapid-acting insulin asparat compared with human insulin in type 2 diabetes patients: an analysis from the Japanese third-party payer perspective. J Med Econ 14: 36–46.
34. Mission JF, Ohno MS, Chung YW, Gaughey AB (2012) Gestational diabetes screening with the new IADPSG guidelines: a cost-effectiveness analysis. Am J Obstet Gynecol 207: 326 e321–329.
35. Law AM, Kelton WD (2000) Simulation Modeling and Analysis: McGraw-Hill Higher Education.
36. Law AM, Kelton WD (2000) Simulation modeling and analysis. Boston: McGraw-Hill, xxi, 760 p. p.
37. Ahlvieht SS KE, Banfi F, Jamieson DJ, Whiteman MK, Kouris AP, et al. (2012) Diabetes trends among delivery hospitalizations in the U.S., 1994–2004. Diabetes Care 33: 768–773.
38. Gethahm D NC, Ananth CV, Chavez MR, Smulian JC (2008) Gestational diabetes in the United States: temporal trends 1989 through 2004. Am J Obstet Gynecol 198.
39. Lydon-Rochelle MT, Holt VI, Cardenas V, Nelson JC, Easterling TR, et al. (2005) The reporting of pre-existing maternal medical conditions and complications of pregnancy on birth certificates and in hospital discharge data. Am J Obstet Gynecol 193: 123–134.
40. Brunner Huber LR (2007) Validity of self-reported height and weight in women of reproductive age. Matern Child Health J 11: 137–144.
41. Lederman SA, Paxton A (1998) Maternal reporting of prepregnancy weight and birth outcome: consistency and completeness compared with the clinical record. Matern Child Health J 2: 123–126.
42. Park S, Sappenfield WM, Bish C, Benzyl DM, Goodman D, et al. (2011) Reliability and validity of birth certificate prepregnancy weight and height among women enrolled in prenatal WIC program. Florida, 2005. Matern Child Health J 15: 851–859.
43. Oken E, Taveras EM, Kleinman KP, Rich-Edwards J, Gillman MW (2007) The reporting of pre-existing maternal medical conditions and complications of pregnancy on birth certificates and in hospital discharge data. Am J Obstet Gynecol 196: 322 e321–328.
44. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaoavindr U, et al. (2008) Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 358: 1901–2002.
45. Narayan KM, Boyle JP, Thompson TJ, Sorenson SW, Williamson DF (2003) Lifetime risk for diabetes mellitus in the United States. JAMA 290: 1884–1890.
46. O’Sullivan JB, Gellis SS, Dandrow RV, Tenney BO (2003) The potential diabetic and her treatment in pregnancy. Obstet Gynecol 102: 7.