Persistence of Risk for Type 2 Diabetes After Gestational Diabetes Mellitus

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EPIDEMIOLOGY/HEALTH SERVICES RESEARCH

OBJECTIVE

Gestational diabetes mellitus complicates ∼6% of pregnancies and strongly predicts subsequent type 2 diabetes. It has not been fully elucidated how risk depends on the number of affected pregnancies or how long the excess risk persists.

RESEARCH DESIGN AND METHODS

We assessed reproductive histories in relation to risk of type 2 diabetes using a nationwide cohort of 50,884 women. Among participants who initially did not have diabetes, 3,370 were diagnosed with diabetes during 10 years of follow-up. We used Cox proportional hazards models that allowed risk to depend on age, cumulative number of pregnancies with gestational diabetes mellitus, and time since the most recent affected pregnancy, adjusting for BMI, educational level, and race/ethnicity.

RESULTS

History of one or more pregnancies with gestational diabetes mellitus predicted elevated age-specific risk of type 2 diabetes, with a hazard ratio of 3.87 (95% CI 2.60–5.75) 6–15 years after an affected pregnancy. Risk increased steeply with multiple affected pregnancies. The age-specific associations attenuated over time after an affected pregnancy, with an estimated 24% reduction of the hazard ratio per decade. Risk remained elevated, however, for >35 years.

CONCLUSIONS

Gestational diabetes mellitus predicted markedly increased rates of type 2 diabetes. Relative risk increased substantially with each additional affected pregnancy. The estimated hazard ratio declined with time after a pregnancy with gestational diabetes mellitus but remained elevated for >35 years. Women recalling a history of gestational diabetes mellitus should be screened regularly for type 2 diabetes, even late in life.

Gestational diabetes mellitus (GDM) is defined as hyperglycemia with onset during the second or third trimester of pregnancy in women without a previous diagnosis of non-GDM (1). The estimated per-pregnancy rates of GDM range from 4.6 to 9.2%, depending on the diagnosis strategy and data source (2).

GDM is believed to typically be a result of pancreatic β-cell dysfunction in women with preexisting insulin resistance (3). These deficiencies can progress, which increases a woman's risk of developing type 2 diabetes after pregnancy (4).

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A meta-analysis on this topic estimated that the risk for type 2 diabetes among women with GDM was 10-fold elevated (relative risk 9.51, 95% CI 7.41–12.67) compared with women with a normoglycemic pregnancy (5). Based on this evidence, a diagnosis of GDM during pregnancy may expose an underlying susceptibility to type 2 diabetes and function as a harbinger of future disease risk. This susceptibility is unsurprising since GDM shares risk factors with type 2 diabetes, such as an elevated BMI (6), that tend to persist or worsen in subsequent pregnancies. Since the risk of GDM recurrence increases (7) if a woman experiences more than one pregnancy with GDM, it is plausible that risk of type 2 diabetes would also increase after multiple affected pregnancies.

Type 2 diabetes is a global problem, affecting an estimated 463 million adults worldwide (8). Epidemiological evidence suggests that it can be prevented or delayed if appropriate interventions are implemented among people at high risk (9–11). Women affected by GDM during pregnancy comprise an easily identifiable population that could potentially benefit from early preventive lifestyle interventions. Therefore, it is of great public health importance to identify women at greatest risk of developing type 2 diabetes following a pregnancy with GDM and to study the persistence of this risk over time. In turn, knowing the persistence of risk could clarify how long women and physicians should pay special attention to diabetes screening postpartum. Consequently, the main objectives of this study are to *1*) evaluate how the risk of type 2 diabetes varies with BMI and the cumulative number of pregnancies affected by GDM and *2*) investigate how the age-specific relative risk of type 2 diabetes changes over time after a GDM diagnosis.

RESEARCH DESIGN AND METHODS

Study Population

The Sister Study (12) is a prospective observational cohort study that investigates environmental and genetic contributors to breast cancer and other health conditions. Between 2003 and 2009, the study enrolled 50,884 women aged 35–74 years who resided in the U.S., including Puerto Rico. Each participant had never been diagnosed with breast cancer but had a full or half-sister with a history of breast cancer. At enrollment, participants completed a computer-assisted telephone interview that ascertained sociodemographic and lifestyle characteristics, environmental exposures, and reproductive and medical history, including history of GDM and type 2 diabetes. Trained examiners collected blood samples, obtained written informed consent, and took anthropometric and blood pressure measurements. The study is overseen by the institutional review board of the National Institutes of Health (Bethesda, MD).

Enrolled women complete brief health updates annually (about recent diagnoses), with response rates of ∼90% throughout follow-up. Women in the Sister Study cohort had a mean age of 55 years at enrollment. We excluded 3 women who withdrew from the study and 57 who reported breast cancer before completing enrollment (and were therefore ineligible). Additionally, 822 women provided inconsistent information about their type 2 diabetes status. We considered these women to be prevalent cases ($n = 160$) if they self-reported taking one or more type 2 diabetes–specific medications (insulin, metformin, and/or oral nonbiguanide medications), and incident cases ($n = 103$) if they reported using these medications after enrollment only. We excluded two women for whom we could not infer timing of their type 2 diabetes diagnosis. The remaining 557 were considered to not have diabetes at enrollment. A total of 3,222 women who had diabetes at enrollment were excluded, and 129 women who reported having been pregnant but did not report GDM were excluded. The final analytical sample was 47,471 women. Of note, although the Sister Study comprises a cohort of women with a family history of breast cancer, there was no overall association between type 2 diabetes and breast cancer in this cohort (13).

Exposure, Outcome, and Covariate Assessment

Information on participants' history of GDM was ascertained at enrollment. For each of their pregnancies, participants were asked whether they had had pregnancy-related diabetes or an abnormal glucose tolerance test during the pregnancy (which was coded as GDM). Pregnant women were only categorized as having GDM if they reported no history of any nonpregnant diabetes beforehand. Although the follow-up questionnaires asked about pregnancies that occurred after enrollment, we did not ascertain GDM status for those pregnancies. A total of 514 pregnancies (<1%) occurred after study enrollment.

We assessed the risk of type 2 diabetes ($n = 3,370$ incident cases) using self-reported physician-diagnosed type 2 diabetes status or self-reported type 2 diabetes medication use, as reported on each follow-up questionnaire. Information about age, education level (less than high school degree, some college but no degree, associate's or technical degree, bachelor's degree, master's degree, or doctoral degree), and race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, or other [American Indian or Alaskan Native, Asian, Native Hawaiian, other Pacific Islander]) was collected on the baseline questionnaire, and participants were asked about their BMI during their 30s. We also measured participants' BMI at enrollment (underweight/normal weight <25.0 kg/m^2, overweight 25.0–29.9 kg/m^2, obese ≥ 30.0 kg/m^2).

Statistical Analysis

We described cohort characteristics for categorical variables by the count (%) and for continuous variables by mean (SD) or median (25th–75th percentile), according to their distribution. We used age as the primary time scale in all incidence models, with person-time beginning at a participant's age at enrollment. Participants were followed until type 2 diabetes diagnosis, with censoring at age of death, age at loss to follow-up, or age in September 2018 (data release 8.1), whichever came first.

In our analyses, we adjusted for race/ethnicity (categorical, 15 missing values), education level (categorical, 11 missing values), and BMI (categorical, 402 missing values for BMI during the participants' 30s and 12 missing values for baseline BMI). These confounders were selected a priori using directed acyclic graphs (14).

Multivariable Cox proportional hazard models were used to estimate the hazard ratios (HRs) and 95% CIs for type 2 diabetes as associated with history of GDM, both as a dichotomous and as categorized variable based on the time-

dependent cumulating number of GDM occurrences. The main effects of GDM were first fitted in Cox models that presumed the HRs remain fixed over time. We then relaxed that assumption by permitting the GDM HR for type 2 diabetes to change with the time elapsed since the most recent pregnancy with GDM. To accomplish this, we included a time-dependent indicator variable for GDM (set permanently to 0 for nulliparous women and parous women who never had a pregnancy with GDM) as well as a time-varying interaction term between the GDM indicator and time elapsed since last GDM diagnosis (which is 0 at age of first pregnancy GDM). In this way, the estimated HR for the association between GDM and incident type 2 diabetes was allowed to change over time. When modeled as a continuous variable, we included both a linear and a quadratic term, using a likelihood ratio test to assess whether the quadratic term was needed to improve the fit. As an alternative approach, we stratified by time elapsed in categories 0–5 years, 6–15 years, 16–25 years, 26–35 years, and >35 years since the most recent GDM diagnosis. In models that include the time since diagnosis interaction term, the exponentiated coefficient of the GDM indicator variable estimates the initial age-adjusted HR soon after a GDM diagnosis. Since BMI at the time of enrollment may have been influenced by previous GDM and consequently may be a mediator of the GDM-type 2 diabetes association, we ran sensitivity analyses adjusting instead for self-reported average BMI at ages 30–39 years (our best proxy for pregestational BMI).

Potential effect modification by race/ethnicity was evaluated using an interaction term between GDM and race/ethnicity; likelihood ratio statistics were used to assess whether the inclusion of the interaction term improved model fit, which would indicate heterogeneity. Stata 16 software (StataCorp, College Station, TX) was used for all statistical analyses.

RESULTS

Participant characteristics by history of GDM at enrollment are listed in Table 1. A total of 1,414 women at baseline reported having had at least one pregnancy with GDM. On average, women reporting GDM were slightly younger and had a higher baseline BMI. During follow-up (mean 10.2 years), 3,180 women without a history of GDM (6.9%) and 190 women with GDM (13.4%) developed type 2 diabetes.

Table 1—Baseline characteristics of women with and without GDM (N = 47,471)

Characteristic	Without GDM (n = 46,057)	With GDM (n = 1,414)
Age at enrollment, years	55.6 ± 9.0	51.0 ± 8.0
BMI, kg/m^2	27.4 ± 6.0	28.2 ± 6.6
Number of births	1.9 ± 1.3	2.5 ± 1.1
Age at enrollment, years		
<40	1,937 (4.2)	106 (7.5)
40–50	11,154 (24.2)	559 (39.5)
50–60	18,025 (39.1)	564 (39.9)
≥60	14,941 (32.4)	185 (13.1)
Race		
Non-Hispanic White	39,094 (84.9)	1,121 (79.3)
Non-Hispanic Black	3,705 (8.1)	135 (9.5)
Hispanic	2,094 (4.5)	110 (7.8)
Other	1,149 (2.5)	48 (3.4)
Education		
High school or less	6,841 (14.9)	195 (13.8)
Some college but no degree	8,871 (19.3)	273 (19.3)
Associate's or technical degree	6,484 (14.1)	231 (16.4)
Bachelor's degree	12,612 (27.4)	393 (27.8)
Master's or doctoral degree	11,238 (24.4)	321 (22.7)
BMI, kg/m^2		
<24.9	18,477 (40.1)	535 (37.8)
25–29.9	14,885 (32.3)	421 (29.8)
≥30	12,683 (27.5)	458 (32.4)
Parity		
Nulliparous	8,673 (18.8)	0
1	6,656 (14.5)	184 (13.0)
2	16,968 (36.8)	638 (45.1)
≥3	13,760 (29.9)	592 (41.9)
Type 2 diabetes		
No	42,877 (93.1)	1,224 (86.6)
Yes	3,180 (6.9)	190 (13.4)

Data are mean ± SD or n (%). The following variables had missing data: race (15 without GDM and 0 with GDM), education level (11 without GDM and 1 with GDM), and BMI (12 without GDM and 0 with GDM).

Results from the Cox proportional hazard models (Table 2) showed an overall estimated HR of 2.50 (95% CI 2.15–2.91) for the association between history of any GDM (as reported at start of follow-up) and a later diagnosis of type 2 diabetes. The strength of the association decreased over time, with the HR after GDM declining ∼24% with each passing decade (HR multiplier per decade since GDM 0.76, 95% CI 0.66–0.88). However, the risk remained elevated even after 35 years. With stratification according to intervals of time since GDM, the HRs were 3.87 (95% CI 2.60–5.75) within 6–15 years, 3.50 (95% CI 2.79–4.40) within 16–25 years, 1.95 (95% CI 1.46–2.61) within 26–35 years, and 1.62 (95% CI 1.12–2.33) after 35 years. We were not able to estimate an HR for the first 5 years after GDM, since most women enrolled after that.

The estimated risk of developing type 2 diabetes increased steeply with the number of pregnancies with GDM (Table 3). Women with more than three affected pregnancies who were within 6–15 years of their last GDM diagnosis had an approximately sevenfold increased risk (HR 7.15, 95% CI 3.71–13.78) of developing type 2 diabetes compared with those without a GDM diagnosis. Their HR was estimated as 3.08 (95% CI 1.60–5.94) after 35 years. Results from the sensitivity analyses adjusting by self-reported average

Table 2—Prospective association between GDM and incident type 2 diabetes (n = 46,529)

	Ever having pregnancy with GDM, HR (95% CI)		Time since last pregnancy with GDM, HR (95% CI)
	No GDM	GDM	
Person-years	462,042	10,958	—
Participants, *n*	45,357	1,172	—
Model 1: model with no time since GDM interaction	1 (ref)	2.50 (2.15–2.91)	—
Model 2: model with time since GDM interaction term†			
GDM effect†	1 (ref)	5.07 (3.36–7.65)	0.76 (0.66–0.88)
Model 3: model stratified by time since last pregnancy with GDM, years			
6–15	1 (ref)	3.87 (2.60–5.75)	—
16–25	1 (ref)	3.50 (2.79–4.40)	—
26–35	1 (ref)	1.95 (1.46–2.61)	—
>35	1 (ref)	1.62 (1.12–2.33)	—

Adjusted for race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other [American Indian or Alaskan Native, Asian, Native Hawaiian, other Pacific Islander]), BMI at enrollment (under/normal weight <25 kg/m^2, overweight 25 to <30 kg/m^2, obese ≥30 kg/m^2), and education level (less than high school degree, some college but no degree, associate's or technical degree, bachelor's degree, master's degree, or doctoral degree). ref, reference. †HR for time since GDM interaction term is 0.76 (95% CI 0.66–0.88) per decade of time elapsed. The HR goes down by 24% with every decade of time elapsed.

BMI at ages 30–39 years instead of baseline BMI showed little difference in the observed results (Supplementary Tables 1 and 2).

We estimated the cumulative risk of type 2 diabetes as a function of age among those without diabetes at age 40 years based on a simple Kaplan-Meier lifetable analysis of the prospective data stratified by baseline BMI (Fig. 1). In all instances, cumulative incidence was considerably higher among participants with GDM than among those without. Among participants with a history of GDM, the cumulative incidence rate of type 2 diabetes by age 80 years in those without diabetes at age 40 years was 67.4% (95% CI 59.0–75.6%) for women with obesity, 44.3% (95% CI 32.8–57.8%) for women who were overweight, and 16.1% (95% CI 9.41–26.8%) for women who were underweight or normal weight (Fig. 1).

CONCLUSIONS

In this large cohort of women, a history of GDM predicted greatly increased rates of type 2 diabetes. We also observed that although the age-adjusted relative risk of type 2 diabetes declined with time since the most recent GDM diagnosis, it remained elevated for >35 years.

GDM often presages the development of type 2 diabetes (5,15–18); previous studies reported at least a 10-fold increased risk associated with a recent affected pregnancy. Based on a systematic review of studies in women as late as 28 years after their pregnancy with GDM (16), the cumulative incidence of type 2 diabetes increases steeply within the first 10 years after delivery but appears to plateau afterward. Such a pattern suggests that there is no longer an increased risk after 10 years. However, those estimates were based on contacting women who had participated much earlier in studies of GDM. Loss to follow-up and nonparticipation may have depended on whether the woman had developed type 2 diabetes. By contrast, in our prospective study of incident type 2 diabetes, we relied on actuarial methods and found that the incidence was elevated >35 years after the last pregnancy with GDM. More consistent with our findings, a recent study (19) found that the crude cumulative incidence of type 2 diabetes increased linearly up to 23 years. Our results complement and expand on that finding by providing time-specific HR estimates, adjusted for BMI, ethnicity, and education level, with follow-up that included ongoing times >35 years after the last GDM diagnosis.

To our knowledge, the importance of a GDM history when there have been multiple affected pregnancies has not been carefully examined previously. In our prospective study, the risk increased steeply with the reported number of affected pregnancies. Our results suggest that special emphasis should be placed on providing adequate screening for women who have had GDM, especially those who have had multiple such pregnancies.

Women with a diagnosis of GDM are advised to be screened for diabetes 4–12 weeks postpartum (20) and then screened for type 2 diabetes or prediabetes at least every 3 years (20), but most women with GDM reportedly are not screened after delivery (21). Our finding that women with GDM remain at an elevated risk of developing type 2 diabetes for >35 years should be a call to action that motivates women who were ever diagnosed with GDM to be screened regularly. Similarly, it should alert health professionals to extend screening programs to target this population.

These findings are biologically plausible. GDM may typically reflect pancreatic β-cell dysfunction in women with preexisting insulin resistance (3). In these women, insulin secretion does not increase appropriately to counteract the insulin resistant state that occurs in the second half of pregnancy (21). These deficiencies may in most cases be progressive, which can plausibly increase a

Table 3—Prospective association between GDM and incident type 2 diabetes, accounting for the number of pregnancies with GDM (n = 46,529)

	Cumulative number of pregnancies with GDM, HR (95% CI)				Time since last pregnancy with GDM, HR (95% CI)
	0	1	2	≥3	
Person-years	462,042	9,011	1,543	405	—
Participants, *n*	45,357	952	173	47	—
Model 1: model with no time since GDM interaction	1 (ref)	2.26 (1.90–2.69)†	3.24 (2.32–4.52)†	4.78 (2.77–8.25)†	—
Model 2: model with time since GDM interaction term‡					
GDM effect‡	1 (ref)	4.48 (2.93–6.87)	6.22 (3.79–10.22)	9.35 (4.84–18.07)	0.77 (0.66–0.89)
Model 3: model stratified by time since last pregnancy with GDM, years					
6–15	1 (ref)	3.46 (2.30–5.21)	4.77 (2.93–7.77)	7.15 (3.71–13.78)	—
16–25	1 (ref)	3.17 (2.48–4.06)	4.37 (3.01–6.35)	6.55 (3.69–11.61)	—
26–35	1 (ref)	1.78 (1.32–2.40)	2.45 (1.60–3.77)	3.67 (2.04–6.63)	—
>35	1 (ref)	1.49 (1.03–2.17)	2.06 (1.29–3.30)	3.08 (1.60–5.94)	—

Adjusted for race or ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other [American Indian or Alaskan Native, Asian, Native Hawaiian, other Pacific Islander]), BMI at enrollment (under/normal weight <25 kg/m^2, overweight 25 to <30 kg/m^2, obese ≥30 kg/m^2), and education level (less than high school degree, some college but no degree, associate's or technical degree, bachelor's degree, master's degree, or doctoral degree). ref, reference. †P for trend < 0.001. ‡HR for time since GDM interaction term is 0.77 (95% CI 0.66–0.89) per decade of time elapsed. The HR goes down by ∼23% with every decade of time elapsed.

woman's risk of overt diabetes after a pregnancy with GDM (4,21). Furthermore, repeated episodes of GDM apparently heighten this risk (22), or perhaps provide stronger evidence for deficiencies in underlying glucose metabolism. It is also possible that GDM itself has deleterious effects on β-cell function.

Congruent with our results, a previous study (22) reported that among women with a history of GDM, a subsequent diagnosis of type 2 diabetes is more likely among those who are obese compared with those at a lower weight. This observation further highlights the need to consider BMI in type 2 diabetes prevention educational campaigns and lifestyle interventions tailored to women with both risk factors to promote weight loss and maintenance of a healthy weight after pregnancy.

Type 2 diabetes incidence is evidently markedly elevated in the first 5 years after a GDM diagnosis (17). Some, but not all, of that is likely due to increased screening following a pregnancy with GDM. On average, women in the Sister Study were past their reproductive age (mean age of 55 years) when they enrolled. Women who had already developed type 2 diabetes before enrollment were excluded from our prospective analysis (n = 3,222).

A limitation of our study was that the history of GDM was self-reported, which could have led to some misclassification of that history. However, a previous study reported 94% agreement between GDM self-report and a physician diagnosis drawn from the medical record (23). Type 2 diabetes was also self-reported, but a previous study reported positive predictive values of 91.8% for self-reported prevalent diabetes and 82.2% for incident diabetes (24). Furthermore, in a sample of ∼2,000 women in the Sister Study who did not report type 2 diabetes at enrollment, 7.7% of those who later reported a diagnosis of type 2 diabetes and 1% of those who did not report incident type 2 diabetes had a hemoglobin A_{1c} ≥6.5% (48 mmol/mol) at baseline, suggesting that undiagnosed type 2 diabetes was not prevalent at enrollment in this cohort (13). Nevertheless, to the extent that some women with GDM were mistakenly classified as unexposed and some type 2 diabetes diagnoses were missed, our estimates may be biased toward the null. We also recognize that the underreporting of GDM may increase as women age and time passes after an affected pregnancy, so in fact, our estimate of the HR for person-time >35 years after the last pregnancy with GDM may underestimate the actual HR. On the other hand, a physician making a screening recommendation also would likely be relying on a woman's self-report, as few would have ready access to obstetric records that are >35 years old. So, the HR based on self-report may be more clinically relevant than one based on actual clinical data.

We only asked participants about their GDM diagnoses before enrollment and would have missed any diagnoses that occurred after enrollment. This would have little impact in our prospective analysis, however, since <1% of women in the cohort had a pregnancy during follow-up. Another limitation is that we do not have data on some covariates that could act as confounders of the relationship between GDM and type 2 diabetes. Specifically, we do not have data on physical activity at a point in time that was relevant for the association under study, and some residual confounding may remain. Additionally, baseline BMI may be a mediator of the GDM-type 2 diabetes association if GDM caused subsequent weight gain. We ran sensitivity analyses where we adjusted the prospective analysis by self-reported average

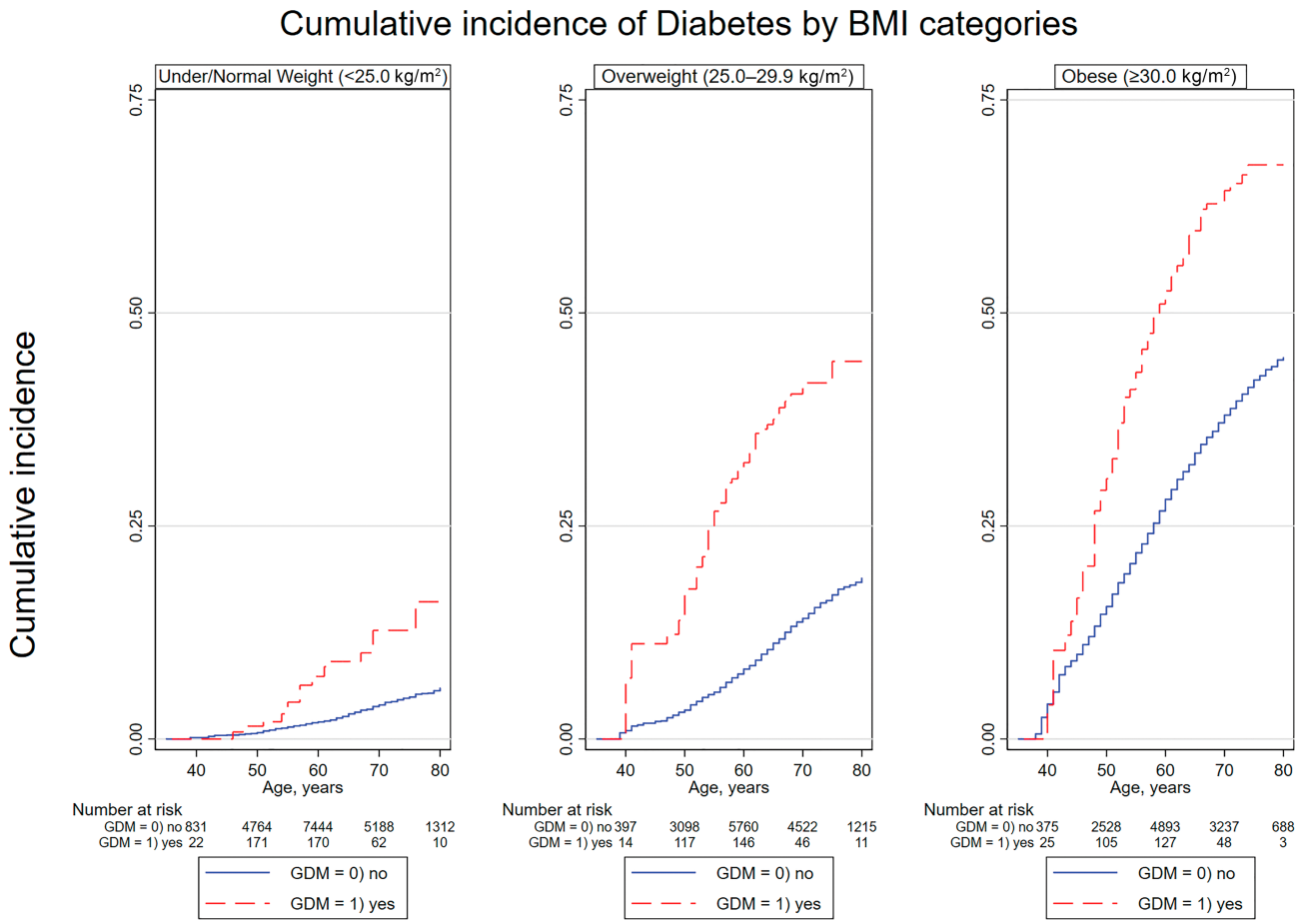

Figure 1—Cumulative incidence of type 2 diabetes for women in the Sister Study cohort by categories of BMI.

BMI at ages 30–39 years (our best proxy for pregestational BMI) instead of adjusting for baseline BMI, and there was little difference in the observed results.

The Sister Study cohort includes only women with a first-degree family history of breast cancer, which could raise the question of generalizability. However, there was no overall association between type 2 diabetes and breast cancer risk in this cohort (13). Also, most of the participants are non-Hispanic White women and highly educated, a group that is at a lower risk of developing GDM and type 2 diabetes (25,26). Despite these limitations, some of the study's strengths lie in the fact that the study had, on average, 10.2 years of follow-up in the prospective analysis, a high retention rate, and a large sample size.

Personalized lifestyle interventions that target women with both a BMI in the overweight or obese category and a history of GDM may be effective in reducing their burden of type 2 diabetes. Additionally, women with a history of GDM, especially those with a history of multiple pregnancies with GDM who also have a BMI in the overweight or obese category, should be screened regularly for type 2 diabetes, even late in life.

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References

1. American Diabetes Association. 2. Classification and diagnosis of diabetes: *Standards of Medical Care in Diabetes-2018*. Diabetes Care 2018;41(Suppl. 1):S13–S27

2. DeSisto CL, Kim SY, Sharma AJ. Prevalence estimates of gestational diabetes mellitus in the United States, Pregnancy Risk Assessment Monitoring System (PRAMS), 2007-2010. Prev Chronic Dis 2014;11:E104

3. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. Int J Mol Sci 2018;19:3342

4. Homko C, Sivan E, Chen X, Reece EA, Boden G. Insulin secretion during and after pregnancy in patients with gestational diabetes mellitus. J Clin Endocrinol Metab 2001;86:568–573

5. Vounzoulaki E, Khunti K, Abner SC, Tan BK, Davies MJ, Gillies CL. Progression to type 2 diabetes in women with a known history of gestational diabetes: systematic review and meta-analysis. BMJ 2020;369:m1361

6. Bao W, Yeung E, Tobias DK, et al. Long-term risk of type 2 diabetes mellitus in relation to BMI and weight change among women with a history of gestational diabetes mellitus: a prospective cohort study. Diabetologia 2015;58:1212–1219

7. Getahun D, Fassett MJ, Jacobsen SJ. Gestational diabetes: risk of recurrence in subse-

quent pregnancies. Am J Obstet Gynecol 2010; 203:467.e1–467.e6
8. Saeedi P, Petersohn I, Salpea P, et al.; IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract 2019;157: 107843
9. Lindahl B, Nilssön TK, Borch-Johnsen K, et al. A randomized lifestyle intervention with 5-year follow-up in subjects with impaired glucose tolerance: pronounced short-term impact but long-term adherence problems. Scand J Public Health 2009;37:434–442
10. Tuomilehto J, Lindström J, Eriksson JG, et al.; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343–1350
11. Ratner RE, Christophi CA, Metzger BE, et al.; Diabetes Prevention Program Research Group. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. J Clin Endocrinol Metab 2008;93:4774–4779
12. Sandler DP, Hodgson ME, Deming-Halverson SL, et al.; Sister Study Research Team. The Sister Study cohort: baseline methods and participant characteristics. Environ Health Perspect 2017; 125:127003
13. Park YM, Bookwalter DB, O'Brien KM, Jackson CL, Weinberg CR, Sandler DP. A prospective study of type 2 diabetes, metformin use, and risk of breast cancer. Ann Oncol 2021;32: 351–359
14. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. Epidemiology 1999;10:37–48
15. Song C, Lyu Y, Li C, et al. Long-term risk of diabetes in women at varying durations after gestational diabetes: a systematic review and meta-analysis with more than 2 million women. Obes Rev 2018;19:421–429
16. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care 2002;25: 1862–1868
17. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 2009;373:1773–1779
18. Lowe WL Jr, Scholtens DM, Lowe LP, et al.; HAPO Follow-up Study Cooperative Research Group. Association of gestational diabetes with maternal disorders of glucose metabolism and childhood adiposity. JAMA 2018;320:1005–1016
19. Auvinen AM, Luiro K, Jokelainen J, et al. Type 1 and type 2 diabetes after gestational diabetes: a 23 year cohort study. Diabetologia 2020;63: 2123–2128
20. American Diabetes Association. 14. Management of diabetes in pregnancy: *Standards of Medical Care in Diabetes-2020*. Diabetes Care 2020;43(Suppl. 1):S183–S192
21. Kim C, Tabaei BP, Burke R, et al. Missed opportunities for type 2 diabetes mellitus screening among women with a history of gestational diabetes mellitus. Am J Public Health 2006;96: 1643–1648
22. Casagrande SS, Linder B, Cowie CC. Prevalence of gestational diabetes and subsequent type 2 diabetes among U.S. women. Diabetes Res Clin Pract 2018;141: 200–208
23. Solomon CG, Willett WC, Rich-Edwards J, et al. Variability in diagnostic evaluation and criteria for gestational diabetes. Diabetes Care 1996;19:12–16
24. Jackson JM, DeFor TA, Crain AL, et al. Validity of diabetes self-reports in the Women's Health Initiative. Menopause 2014;21:861–868
25. Shai I, Jiang R, Manson JE, et al. Ethnicity, obesity, and risk of type 2 diabetes in women: a 20-year follow-up study. Diabetes Care 2006; 29:1585–1590
26. Lawrence JM, Contreras R, Chen W, Sacks DA. Trends in the prevalence of preexisting diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women, 1999-2005. Diabetes Care 2008;31: 899–904