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Changes in Cardiometabolic Risk Factors Before and After Gestational Diabetes: A Prospective Life Course Analysis in CARDIA Women

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Abstract

Objective—We hypothesized that both preconception and post-childbearing patterns of cardiometabolic risk factors may be different for women with gestational diabetes (GDM) compared to women without GDM.

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Conflict of Interest: The authors declared no conflict of interest.

Data Sharing Statement: Study materials, data, and samples from CARDIA are available at <https://www.cardia.dopm.uab.edu/> and through the NHLBI BioLINCC program at <https://biolincc.nhlbi.nih.gov/home/>.

Clinical trial registry: The CARDIA study was registered in the [ClinicalTrial.gov](https://clinicaltrials.gov/) registry with the number [NCT00005130](https://clinicaltrials.gov/ct2/show/study?term=NCT00005130). The original protocol for the study is published in Friedman GD, Cutter GR, Donahue RP, Hughes GH, Hulley SB, Jacobs DR, Jr. et al. CARDIA: study design, recruitment, and some characteristics of the examined subjects.

Methods—Among 1,302 (51% Black) women in the Coronary Artery Risk Development in Young Adults study with births and followed for 30 years, we evaluated changes in cardiometabolic factors (BMI, waist circumference [WC], lipids, blood pressure) during pre-childbearing (prior to the first post-baseline birth) and post-childbearing periods (after the last birth) by GDM status using piecewise linear mixed-models adjusted for socio-demographics, parity and time-varying covariates.

Results—Compared to women who did not develop GDM, weight and WC increases in women who developed GDM (n=152, 12%) were faster (BMI difference +0.12 kg/m² per year [p=0.04]; WC difference +0.28 cm per year [p=0.04]) during the pre-childbearing period, accounting for covariates. This translated to an average of 1.3 kg excess weight gain across 4 years among women with subsequent GDM vs. non-GDM births. In contrast, slopes after childbearing did not differ by GDM status nor were there other cardiometabolic differences.

Conclusions—Women with GDM exhibited an increasing pre-pregnancy pattern of weight gain and central adiposity. Absolute post-childbearing weight was also higher in GDM-affected women but the slope of gain after GDM was not.

Keywords

Gestational diabetes mellitus; Obesity; Pregnancy; Preconception; Weight change; Prospective cohort

Introduction

Gestational diabetes mellitus (GDM), defined as glucose intolerance of variable severity first recognized during pregnancy, develops in 8–20% of all U.S. pregnancies. GDM pregnancy heightens the risk of adverse perinatal outcomes, as well as prediabetes, type 2 diabetes, and cardiovascular disease (CVD), including early atherosclerosis, for both the mother and child.^{1–7} We have previously reported that excess adiposity and impaired metabolic function prior to pregnancy [i.e., prediabetes, higher insulin resistance, and/or low high-density lipoprotein (HDL)-cholesterol] increases the risk of developing GDM more than threefold.⁸ In clinical settings, the identification of cardiometabolic risk before pregnancy is challenging, because routine biochemical screening for abnormal blood glucose and lipids is not currently recommended by the U.S. Preventive Health Task Force before age 40.⁹ Thus, there are significant challenges in identifying women at risk for GDM from among those without recognized risk factors, such as women without a family history of diabetes or within healthy weight categories.

Evaluation of available clinical parameters, such as serial measurements of body weight before pregnancy, may provide valuable GDM risk stratification information. This may be particularly important among normal weight women without a family history of diabetes and those under age 30 years who are typically considered as low risk. Evidence is limited regarding whether changes in overall and regional adiposity (i.e., increasing body weight and waist circumference [WC]) preceding pregnancy increase GDM risk above pre-pregnancy body size or other risk factors. Most studies have evaluated body mass index (BMI) at a single point in time proximate to pregnancy, or in early pregnancy.^{10–12} One

study that evaluated weight change from age 18 years found that a 10 kg or higher gain was associated with a 3.4-fold increase in GDM.¹³ Whether more modest pre-pregnancy weight gain patterns also portend risk, and whether these patterns identify risk among otherwise low risk women is unknown.

It is biologically plausible that weight gain preceding pregnancy may contribute to excess risk for GDM as this may signal an impaired metabolic profile less able to successfully adapt to the transient state of mild insulin resistance that normal pregnancy requires to support fetal growth. While post-GDM weight retention and gain may contribute to progression to type 2 diabetes and CVD,¹⁴ it is unknown if this weight gain trajectory may have initiated prior to pregnancy. This distinction is critical to identify the optimal timing for interventions to prevent GDM and its long term maternal and offspring sequelae.¹⁵ To our knowledge, serial measurements of body anthropometry and cardiometabolic risk factors prior to pregnancy and after delivery have not been evaluated in relation to GDM pregnancy. We set out to address this gap by conducting a life-course study of cardiometabolic risk factors measured before pregnancy and after childbearing. This study evaluated the rate of change in body size (BMI), abdominal adiposity (WC), and CVD risk factors (plasma lipids and blood pressure) during the years preceding and following pregnancy in relation to GDM status. We hypothesized that both preconception patterns and post-childbearing patterns of risk factors may be different in women with GDM. We also hypothesized that these associations will be detectable in women without known GDM risk factors prior to pregnancy, such as family history of diabetes and obesity.

Methods

The Coronary Artery Risk Development in Young Adults (CARDIA) study is a U. S. multi-center study examining the trends and determinants of coronary heart disease risk factors in young black and white adults. In 1985–1986, a total of 5,115 participants (2,787 women) aged 18–30 years (51% black) were recruited from four geographic areas in the U.S.: Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California, and followed at in-person exams up to 30 years after baseline (2015–2016). CARDIA retention has been excellent, including at the year 30 exam (71% of the surviving cohort). Institutional Review Boards at each participating study center approved the study. Written, informed consent was obtained from participants.

Study Population

This study includes 1,302 women without diabetes at CARDIA enrollment and before pregnancy, who gave birth at least once after baseline (Supplemental Figure 1). We excluded 57 women with multi-fetal gestations, 17 women with GDM or diabetes prior to the first birth during follow-up, and 16 women with incomplete delivery date information. CARDIA exam measurements were excluded if they occurred during the childbearing years (between the first and last post-baseline birth) as there were too few exams to evaluate between-pregnancy changes. Exams that occurred while women were pregnant, less than 6 months post-partum, or breast-feeding were also excluded. Among 1,302 women, a total of 8,423 measurements were evaluated either before or after childbearing. The CARDIA study visits,

by design, were every 3–5 years. The pre-childbearing period was, on average, 5.26 years (± 4.34); the median for this pre-childbearing interval 4.17 years (IQR 5.77). During this pre-childbearing period there were, on average 2.42 (± 1.48) study visits; for the post-childbearing period the mean number of study visits was 4.05 ± 1.86 .

Pregnancies and GDM Status

At each exam, participants reported current pregnancy or lactation status, the number of pregnancies and births since the previous exam, and how they ended (termination, miscarriage, and live or stillbirths). Post-baseline births were defined as delivery of a live infant ≥ 20 weeks gestation that was conceived after the baseline CARDIA exam through year 30. For each birth, women reported the length of gestation, multi-fetal gestation, date of delivery, gestational weight gain, infant birth weight, hypertensive disorders of pregnancy, and diabetes during pregnancy (GDM status). Self-report of GDM history was validated previously via abstraction of glucose tolerance test results from prenatal records for a subsample of 165 women who delivered 200 births after CARDIA enrollment. Sensitivity for classification by self-report as ever having GDM was 100 percent (20 of 20), and specificity was 92 percent (134 of 145).⁽²⁾ Women were classified as GDM if they had one or more GDM births; non-GDM women had all non-GDM births. We calculated time from baseline to the first post-baseline birth and maternal age at each delivery. Time of conception was estimated as the delivery date minus the gestational age at delivery.

BMI and Waist Circumference

Certified technicians measured weight, height, and WC using standardized protocols to the nearest 0.1 kg or 0.5 cm in participants wearing light clothing and without shoes. BMI was computed as weight in kilograms divided by height in meters squared and categorized as normal weight ($<25 \text{ kg/m}^2$), overweight ($25\text{--}29.9 \text{ kg/m}^2$), and obese ($\geq 30 \text{ kg/m}^2$). WC was measured midway between the iliac crest and bottom of the rib cage.

Cardiometabolic Risk Factors and Covariates

Plasma lipids and blood pressure were obtained at baseline and follow-up exams using standardized research methodologies. Hypertension was defined as systolic blood pressure $\geq 140 \text{ mm Hg}$ and/or diastolic blood pressure $\geq 90 \text{ mm Hg}$ or self-reported medication use. The metabolic syndrome was defined by the NCEP-ATP III criteria.¹⁶ Homeostasis model assessment of insulin resistance (HOMA-IR) was derived as: $[\text{fasting glucose (mg/dL)} \times \text{fasting insulin (uU/mL)}] / 405$. These measures were not available between baseline and Year 7, therefore trajectories could not be estimated.

Socio-demographic and other characteristics were assessed at baseline: age, race, and physical activity score. The CARDIA Diet History questionnaire assessed dietary intake at baseline, and years 7 and 20.¹⁷ We calculated an *a priori* diet quality score (average of baseline, year 7 and 20), an index of plant based food patterns, as described in detail elsewhere.¹⁸ Categorical variables were race (black, white), smoking, use of blood pressure and lipid lowering medications, onset of the metabolic syndrome, menopause status, and family history of diabetes. Family history of diabetes was based on report of one or more

first degree relatives (father, mother, or siblings) with diabetes at exam years 0, 5, 10, and 25.

Statistical Analysis

Characteristics of women at baseline and at the interval prior to the first birth were compared by GDM status using chi-square statistics and t-tests, as appropriate. Median and interquartile ranges were reported as appropriate. We evaluated CARDIA exams in three periods: pre-childbearing (CARDIA enrollment to the exam prior to conception of the first post-baseline birth), childbearing (conception of the first birth to 6 months after the last birth), and post-childbearing (6 months after last birth to final CARDIA exam completed).

Cardiometabolic risk factors (BMI, WC, plasma lipids, and blood pressure) were evaluated using piecewise linear mixed-models which allowed differing intercepts and slopes for the pre- and post-childbearing epochs. We set the intercept at the end of pre-childbearing and included an indicator to quantify the change in level jumping to the start of post-childbearing. Coefficients of time variables characterized the annual rates of change in risk factors pre-childbearing (years to the end of pre-childbearing) and post-childbearing (years since the start of post-childbearing). Differences in rates of change (slopes) and differences in level change from pre- to post-childbearing (jump) were evaluated according to GDM status by adding corresponding multiplicative terms. All models were adjusted for fixed covariates (age at first post-baseline birth, race, baseline education, length of the CARDIA childbearing period, average a priori diet quality score, family history of diabetes) and time-varying covariates (parity, blood pressure/lipid-lowering medication use, menopause status, smoking status, physical activity level). We also estimated the individual-specific annual changes in BMI (slope) in the pre-childbearing period by combining the random effects and fixed effects of time to estimate a mean pre-childbearing slope (0.24 kg/m² per year). We summarized maternal characteristics according to those below and above this mean to describe features associated with low gain vs. high gain in this period. Models evaluating plasma lipids and blood pressure were subsequently adjusted for time-varying BMI. All p-values presented are for two-sided tests; statistical significance was defined as <0.05 and all analyses were conducted in SAS v9.4. We also examined estimates among women without known pre-pregnancy GDM risk factors (family history of diabetes or obesity).

To isolate birth-specific influences from lifetime experience of GDM, we restricted our analyses to women nulliparous at baseline who had only one post-baseline birth. We also replicated models among women with two or more CVD risk factor measurements to investigate how longitudinal trajectories were impacted by women with only one available measurement.

Results

Of 1,302 women, 152 (11.7%; 7.6 per 100 pregnancies) reported GDM during a post-baseline birth. Women who developed GDM were heavier at baseline, with larger WC, higher fasting glucose, insulin, and triglycerides than women without GDM (Table 1). They also tended to have more births and higher prevalence of hypertensive disorders of pregnancy. Cardiometabolic differences according to GDM history persisted across the

childbearing years when evaluated cross-sectionally (Supplemental Table 1). Women with GDM also reported higher use of hormones, lipid-lowering, and blood pressure medications at some point across these childbearing epochs. When summarized according to those above or below the mean slope of weight gain in the pre-childbearing period, those above the mean were more likely to be younger, of Black race/ethnicity, have a high school education or less, a lower diet quality score, to be obese with a more adverse cardiometabolic profile, and more likely to have GDM (Supplemental Table 2).

Women with subsequent GDM pregnancies gained weight and waist girth more rapidly prior to childbearing compared to women without GDM (BMI slope difference $+0.12 \text{ kg/m}^2$ [se 0.06] per year [$p=0.04$]; WC slope difference $+0.28 \text{ cm}$ [se 0.13] per year [$p=0.04$]), accounting for covariates. To translate these estimates into average change across the pre-childbearing period, we multiplied the estimated annual slope by 4 years, which is the median length of the pre-childbearing period in our population. This translated to an average of 1.3 kg excess weight gain across 4 years among women with subsequent GDM vs. non-GDM births (average 4-year pre-pregnancy gain for women with GDM, 3.8 kg; for women without GDM, 2.5 kg).

BMI and WC were higher in the post-childbearing years among women with GDM than non-GDM births (29.4 vs. 27.3 kg/m^2 at the start of the post-childbearing period; 31.9 vs. 30.0 kg/m^2 at the end of follow up, all $p<0.01$; Supplemental Table 1). These adiposity measures, however, did not increase differentially after childbearing according to GDM status (slope 0.17/year GDM vs. 0.19/year non-GDM, $p=0.41$; Table 2 and Figure 1A–1B). Additional adjustment for hypertensive disorders of pregnancy did not change these findings, and results were similar when replicating our analyses in women with at least two CVD risk factor measurements ($n=1,293$, Supplemental Table 3).

Pre-childbearing increases (slope) in BMI and WC among women with subsequent GDM were detected when restricted to women nulliparous at CARDIA baseline ($n=877$ [GDM, $n=100$, 11.4%]; Supplemental Table 4). To isolate birth-specific influences (rather than the overall childbearing period), we replicated our analysis among nulliparous women with only 1 post-baseline birth ($n=317$ [GDM, $n=24$, 7.6%]). Results in this group regarding pre-childbearing annual increases in BMI and WC were maintained (Figure 1C–1D). In additional sensitivity analyses, the rate of pre-childbearing weight gain associated with GDM among women without a family history of diabetes was 88% higher than among those with no GDM (GDM, 0.32 vs. non-GDM, 0.17 Table 3). Excess gain (increasing slope) prior to childbearing also was higher among non-obese women who developed GDM compared to those who did not develop GDM (GDM, 0.32 vs. non-GDM, 0.14, $p=0.08$) but these differences were not statistically significant.

There were no other slope differences (increases or decreases) of cardiometabolic risk factors detected before or after GDM pregnancies (Table 2 and Supplemental Figure 2). For example, although total cholesterol, HDL-cholesterol and low-density lipoprotein (LDL)-cholesterol on average dropped from the end of the pre-childbearing to the beginning of the post-childbearing periods and triglycerides increased, these changes did not differ according to GDM history..

Discussion

Our study pinpoints pre-childbearing patterns of overall weight gain and increasing central adiposity as risk factors for developing GDM during pregnancy. Importantly, these patterns persisted after delivery and yet did not differentially increase after GDM births. Thus, the pre-pregnancy cardiometabolic profile is a critical time for accrual of risk and could be a key time for lifestyle interventions to mitigate GDM risk and improve long-term health. Our data demonstrate that this pre-pregnancy pattern of weight gain may be particularly important for those without a family history of diabetes. Therefore, patterns of weight gain before pregnancy may inform risk stratification among women without clinical risk factors for GDM.

Women who develop GDM exhibit pancreatic beta cell defects resulting in insufficient insulin secretion to meet the superimposed demands of pregnancy on glucose metabolism. Obesity before pregnancy is a key risk factor for GDM. However, development of GDM among non-obese women is less understood. This is important, as half of GDM cases occur in this group.¹⁹ Although overweight status is a known risk factor for GDM, our data suggest that pre-pregnancy patterns of weight gain may discriminate a group with higher GDM risk. These findings were also true for women without a family diabetes history. Prospective clinical data on longitudinal changes in overall and central adiposity, perhaps increasingly available via the electronic medical record, may be useful to target lifestyle interventions to prevent future GDM.

Few studies have evaluated pre-pregnancy weight change in relation to GDM risk. One study evaluated weight change from a single time point many years prior to conception (i.e., self-reported weight at age 18 y) in relation to the future risk of GDM.⁸ This study revealed that weight gain of 10 kg or more since age 18 was associated with a 3.4-fold higher risk of GDM pregnancy compared to women who gain 2.5 kg in this pre-pregnancy interval.¹³ An earlier report from the Nurses' Health Study II detected a linear increase in GDM risk as pre-gravid weight gain increased from 5 to more than 20 kg, with GDM risks increasing 1.67 to 3.56-fold compared to women who gained less than 5 kg since age 18.²⁰ However, in both of these prior studies, the time interval prior to pregnancy varied, pre-pregnancy data were recalled, and the study populations were almost exclusively white. Our study supports and extends these findings in several important ways. First, we were able to disentangle pre-childbearing and post-childbearing patterns of gain, all results are based on research measures of cardiometabolic risk factors rather than recalled weight, and the CARDIA cohort by design includes balanced numbers of Black and White women. Our results suggest that yearly weight gain patterns in the pre-pregnancy period are particularly important, and provide ranges associated with GDM risk. For example, on average women in our study who developed GDM gained about 1 kg/year compared to almost half that among women who did not develop GDM. It is noteworthy that unlike BMI and waist circumference, changes in other pre-childbearing cardiometabolic risk factors were not related to GDM risk. It could be that weight gain is more directly related to metabolic impairments known to be implicated in GDM.

Randomized controlled trials to reduce gestational weight gain among overweight or obese women have had limited efficacy in preventing GDM.^{21,22} Our data sheds new light on the importance of the pre-childbearing period and supports efforts to consider interventions in the preconception period to promote weight loss, prevent weight gain, and improve metabolic profiles. Our findings demonstrate that, apart from the known clinical risk factors such as family history of diabetes and prepregnancy obesity, weight gain patterns prior to pregnancy may be an efficient and robust indicator of metabolic dysregulation linked to GDM risk. Prevention of weight gain at all stages of life are beneficial, and our data highlights that the pre-childbearing years may be of importance for pregnancy health and long-term health. It is noteworthy that although the absolute values for post-childbearing BMI and waist circumference were higher in GDM-affected women, the rate of change was similar to that of women without GDM. Taken together with the pre-childbearing slope differences, it appears that steeper increases in BMI and waist circumference before GDM pregnancies may have lasting effects.

Limitations of our study include maternal recall of GDM, although women reported GDM with high reliability. We had no cardiometabolic measures during pregnancy including glucose tolerance and GDM treatment. We also lacked cardiometabolic measures between each birth, and therefore the childbearing years were condensed into one period, restricting our ability to study other relevant reproductive factors such as lactation. Cardiorespiratory fitness was not available for each of the necessary years and therefore could not be studied as a serial covariate, though we recently showed that it is a stronger predictor of future GDM than physical activity.²³ Our models also only examined a linear trend in risk factors, although for weight gain and WC this is a reasonable assumption. Although we conducted a sensitivity analysis restricted to nulliparous women with only one birth, we recognize that this group may not be generalizable to all other women if that had only one birth. Major strengths of our study include the longitudinal design with serial standardized measures of anthropometry, plasma lipids, and blood pressure in women both before and after pregnancies every two to five years during the 30-year follow-up period. We were therefore able to distinguish and exclude pre-gestational diabetes from GDM during pregnancy. Another strength is the young age of CARDIA women who delivered pregnancies during the period (1986–2006) when universal screening and treatment for GDM was routine in clinical practice. The percentage of GDM deliveries (7.6 per 100 pregnancies) in CARDIA is comparable to the prevalence in the U.S. population.

To our knowledge, this is the first longitudinal study to examine life course changes in cardiometabolic risk factors from pre-pregnancy to after pregnancy weight gain according to GDM. Our findings provide strong evidence that pre-pregnancy weight gain contributes to the risk of GDM even accounting for demographic and lifestyle factors. This excess risk was detected among those without known GDM risk factors such as family history of diabetes, and the pattern of differential gain prior to conception persisted in the years after GDM but did not further increase. Therefore, patterns of weight gain may help identify women with excess GDM risk. In addition, GDM prevention efforts should be focused on weight maintenance prior to conception to improve pregnancy outcomes and potentially long-term cardiometabolic health in women. This is important, as GDM is a strong risk factor for later life diabetes and prevention of GDM may therefore have lifelong benefit.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is already known on this subject?

- Obesity is a risk factor for gestational diabetes
- Women with gestational diabetes also have excess weight gain after delivery

What are the new findings?

- Patterns of weight gain prior to conception are related to risk of gestational diabetes
- Absolute weight gain after gestational diabetes is higher than non-GDM, but the weight gain slope is similar suggesting that higher rates of gain prior to pregnancy have long term effects

How might the results change the direction of research or the focus of clinical practice?

- Weight management during the reproductive years, before pregnancy, will be important to reduce risk for gestational diabetes
- Because of the importance of preconception weight gain, primary care physicians will play an important role in improving pregnancy health

Figure 1.
Gestational Diabetes Mellitus Life Course Changes Among Women

Table 1.

Maternal characteristics by GDM status of all post-baseline births.

Characteristics	Any GDM Deliveries (N=152)	Non-GDM Deliveries (N=1150)	P-value
<i>Baseline</i>			
Age, year (SD)	24.3 (4.0)	23.9 (3.7)	0.27
Black, n (%)	73 (48.0)	585 (50.9)	0.51
Education, n (%)			0.43
High school or less	49 (32.2)	423 (36.8)	
Some college	91 (59.9)	624 (54.3)	
College education	12 (7.9)	103 (9.0)	
Physical activity level, median exercise units (IQR)	297.0 (295.5)	294.0 (322.0)	0.72
A priori diet quality score, mean (SD)	64.7 (12.7)	63.7 (13.7)	0.39
Ever smoking, n (%)	64 (42.1)	406 (35.3)	0.10
BMI classification, n (%)			<0.01
Normal	96 (63.2)	845 (73.7)	
Overweight	29 (19.1)	188 (16.4)	
Obese	27 (17.8)	114 (9.9)	
BMI, kg/m ² (SD)	25.0 (6.4)	23.5 (4.8)	<0.01
Waist circumference, cm (SD)	75.3 (13.3)	72.0 (9.6)	<0.01
Systolic blood pressure, mm Hg (SD)	106.3 (9.6)	105.6 (9.1)	0.41
Diastolic blood pressure, mm Hg (SD)	66.7 (8.5)	65.7 (8.7)	0.23
Plasma lipids, mg/dL (SD)			
Total cholesterol	178.9 (35.7)	176.2 (32.1)	0.34
HDL-C	54.6 (13.2)	56.0 (12.7)	0.21
LDL-C	109.8 (33.8)	107.4 (29.6)	0.36
Triglycerides, median mg/dL (IQR)	64.0 (31.0)	57.0 (34.0)	<0.01
Fasting serum glucose, mg/dL (SD)	81.1 (9.6)	79.1 (7.3)	<0.01
Fasting serum insulin, μ U/mL (SD)	12.8 (10.0)	10.4 (7.0)	<0.01
HOMA-IR, median (IQR)	2.1 (1.8)	1.7 (1.3)	<0.01
Metabolic syndrome, n (%)	4 (2.6)	9 (0.8)	0.06
Family history of diabetes, n (%)	33 (21.7)	162 (14.1)	0.01
<i>Reproductive characteristics</i>			
Age at menarche, year (SD)	12.5 (1.5)	12.7 (1.5)	0.15
Nulliparous, n (%)	100 (65.8)	777 (67.6)	0.66
Number of post-baseline births, n (%)			0.04
One	54 (35.5)	531 (46.2)	
Two	70 (46.1)	423 (36.8)	
More than two	28 (18.4)	196 (17.0)	
Hypertensive disorders of pregnancy, n (%)	47 (30.9)	230 (20.0)	<0.01
Length of the childbearing period, year (SD)	4.5 (3.8)	3.9 (3.6)	0.09

Abbreviations: SD, standard deviation; IQR, interquartile range; GDM, gestational diabetes mellitus; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance.

P-values were based on t-test or Kruskal-Wallis test for continuous variables and chi-square test or Fisher's exact test for categorical variables.

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Table 2.

Adjusted mean difference in annual rates of change (i.e., slopes) in pre- and post-childbearing periods, between women with and without GDM

	Pre-childbearing rate of change				Post-childbearing rate of change			
	GDM		Non-GDM		GDM		Non-GDM	
	Mean (SE)	Mean (SE)	Mean (SE)	P-value	Mean (SE)	Mean (SE)	Mean Diff (SE)	P-value
Systolic BP (mm Hg)	-0.08 (0.14)	-0.04 (0.05)	-0.04 (0.15)	0.81	0.80 (0.08)	0.67 (0.03)	0.13 (0.08)	0.09
Diastolic BP (mm Hg)	0.28 (0.13)	0.10 (0.05)	0.18 (0.13)	0.18	0.28 (0.06)	0.22 (0.02)	0.06 (0.06)	0.29
BMI (kg/m ²)	0.35 (0.05)	0.23 (0.02)	0.12 (0.06)	0.04	0.17 (0.02)	0.19 (0.01)	-0.02 (0.03)	0.41
Waist circumference (cm)	0.82 (0.13)	0.53 (0.05)	0.28 (0.13)	0.04	0.51 (0.05)	0.54 (0.02)	-0.03 (0.06)	0.59
Total cholesterol (mg/dL)	-0.14 (0.38)	-0.06 (0.13)	-0.09 (0.41)	0.83	1.28 (0.15)	1.21 (0.06)	0.07 (0.15)	0.62
HDL cholesterol (mg/dL)	0.31 (0.15)	0.34 (0.05)	-0.03 (0.16)	0.83	0.73 (0.07)	0.71 (0.03)	0.02 (0.07)	0.78
LDL cholesterol (mg/dL)	-0.55 (0.35)	-0.47 (0.12)	-0.07 (0.37)	0.84	0.46 (0.13)	0.35 (0.06)	0.11 (0.14)	0.42
Triglycerides (log mg/dL) *	0.000 (0.006)	-0.001 (0.002)	0.001 (0.006)	0.87	0.009 (0.002)	0.011 (0.001)	-0.003 (0.002)	0.19

Abbreviations: SE, standard error; GDM, gestational diabetes mellitus; BP, blood pressure; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Final models adjusted for race, age at the 1st post-baseline birth, length of childbearing period, baseline education, average diet score, family history of diabetes, and time-varying parity, smoking, physical activity, high blood pressure medication use (only for BP models) or lipids lowering medication use (only for lipids models), and BMI (except for BMI and waist circumference models).

* Estimated G matrix is not positive definite, but results were comparable when removing slopes from random effects.

Annual rate of change (slope) in BMI and Waist Circumference from pre- to post- childbearing period in cardiometabolic risk factors, without known GDM risk factors.

Table 3.

	N (GDM %)	Pre-childbearing rate of change				Post-childbearing rate of change			
		GDM		Non-GDM		GDM		Non-GDM	
		Mean (SE)	Mean (SE)	Mean Diff (SE)	P-value	Mean (SE)	Mean (SE)	Mean Diff (SE)	P-value
BMI									
a. No family history diabetes	713 (8.7%)	0.32 (0.08)	0.17 (0.02)	0.16 (0.08)	0.04	0.23 (0.04)	0.19 (0.01)	0.05 (0.04)	0.26
b. Prepregnancy BMI <30 k/m ²	1057 (10.5%)	0.23 (0.06)	0.14 (0.02)	0.08 (0.06)	0.14	0.18 (0.02)	0.21 (0.01)	-0.03 (0.03)	0.33
Waist circumference									
a. No family history diabetes	713 (8.7%)	0.67 (0.18)	0.38 (0.06)	0.29 (0.18)	0.11	0.65 (0.09)	0.54 (0.03)	0.11 (0.09)	0.22
b. Prepregnancy BMI <30 k/m ²	1057 (10.5%)	0.52 (0.13)	0.35 (0.04)	0.17 (0.14)	0.20	0.55 (0.06)	0.57 (0.02)	-0.02 (0.06)	0.72

Abbreviations: SE, standard error; GDM, gestational diabetes mellitus; BMI, body mass index.

a. adjusted for race, age at the 1st post-baseline birth, length of childbearing period, baseline education, average diet score, and time-varying parity, smoking, physical activity.

b. adjusted for race, age at the 1st post-baseline birth, length of childbearing period, baseline education, average diet score, family history of diabetes, and time-varying parity, smoking, physical activity.