HHS Public Access

Author manuscript

Int J Obes (Lond). Author manuscript; available in PMC 2024 April 01.

Published in final edited form as:

Int J Obes (Lond). 2024 March ; 48(3): 414–422. doi:10.1038/s41366-023-01441-y.

Maternal gestational diabetes and childhood adiposity risk from 6 to 8 years of age:

Maternal GDM and childhood adiposity

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Abstract

Background/objective: Previous studies found conflicting results on the association between maternal gestational diabetes mellitus (GDM) and childhood overweight/obesity. This study was to assess the association between maternal GDM and offspring's adiposity risk from 6 to 8 years of age.

Methods: The present study longitudinally followed 1,156 mother-child pairs (578 GDM and 578 non-GDM) at 5.9±1.2 years postpartum and retained 912 mother-child pairs (486 GDM and 426 non-GDM) at 8.3±1.6 years postpartum. Childhood body mass index (BMI), waist circumference, body fat and skinfold were measured using standardized methods.

Results: Compared with the counterparts born to mothers with normal glucose during pregnancy, children born to mothers with GDM during pregnancy had higher mean values of adiposity indicators (waist circumference, body fat, subscapular skinfold and suprailiac skinfold) at 5.9 and 8.3 years of age. There was a positive association of maternal GDM with changes of childhood adiposity indicators from the 5.9-year to 8.3-year visit, and β values were significantly larger than zero: +0.10 (95% CI: 0.02-0.18) for z score of BMI for age, +1.46 (95% CI: 0.70-2.22) cm for waist circumference, +1.78% (95% CI: 1.16%-2.40%) for body fat, +2.40 (95% CI: 1.78-3.01) mm for triceps skinfold, +1.59 (95% CI: 1.10-2.09) mm for subscapular skinfold, and +2.03 (95% CI: 1.35-2.71) mm for suprailiac skinfold, respectively. Maternal GDM was associated with higher

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Author Contributions

WL and GH conceived and designed the study. LW, HL, SZ, WL and JL performed the fieldwork and collected data. WL and GH performed the statistical analysis, interpreted the data, and drafted the article. XY, ZY and AS provided major comments to the manuscript. All authors contributed to the article and approved the submitted version. WL and GH were responsible for the integrity of the work as a whole.

Declaration of interest

All authors have no conflicts of interest.

risks of childhood overweight/obesity, central obesity, and high body fat (Odd ratios 1.41-1.57 at 5.9 years of age and 1.73-2.03 at 8.3 years of age) compared with the children of mothers without GDM.

Conclusions: Maternal GDM was a risk factor of childhood overweight/obesity at both 5.9 and 8.3 years of age, which was independent from several important confounders including maternal pre-pregnancy BMI, gestational weight gain, children's birth weight and lifestyle factors. This significant and positive association became stronger with age.

Introduction

Childhood overweight and obesity is one global public health challenge [1]. The global age-standardized prevalence of obesity increased from 0.7% in 1975 to 5.6% in 2016 in girls, and from 0.9% in 1975 to 7.8% in 2016 in boys [2]. Childhood obesity is associated with adult weight status and morbidity, such as cardiovascular diseases and type 2 diabetes [3, 4]. Therefore, identifying and counteracting modifiable risk factors is essential for timely prevention of obesity in children.

The etiology of obesity is complex and multifactorial. Gestational diabetes mellitus (GDM), defined as glucose intolerance with onset or first recognition during pregnancy, has continued to increase nowadays with its prevalence of 14.0% in 2021 [5, 6]. Intrauterine exposure to GDM might play an important role in developing obesity in the childhood and adulthood. Although many studies have provided evidence to support the association of maternal GDM with childhood adiposity, others did not [7–9]. Until now, there are three meta-analyses investigating the association between maternal GDM and offspring's overweight at different developmental stages and the results are quite different [10–12]. The inconsistent findings of these meta-analyses may be partially due to small sample sizes, especially GDM cases, and inadequate control for major confounders (maternal pre-pregnancy body mass index [BMI], children's dietary intake, and physical activity, etc.) [10–12]. Moreover, most of original studies in these three meta-analyses used BMI as an indicator to evaluate obesity/overweight. However, adiposity is excess adipose tissue but not excess weight, and BMI is limited as an indicator of body composition because it reflects the general weight without partitioning body fat, lean mass and bone mass [13]. Alternative metrics include waist circumference that provides a simple method to measure central fat, body fat percent (a direct reflection of overall obesity), and skinfold thickness (conventionally used to classify an individual in terms of relative fat or to evaluate specific subcutaneous tissue fat) [14]. Thus, studies on the impact of maternal GDM on children's growth and development, especially using both BMI and other indicators of adiposity including waist circumference, body fat percent and skinfolds to reflect obesity, are needed.

In addition, most of original studies in three meta-analyses assessed the association of maternal GDM with offspring's overweight at a single age point, and very few studies have assessed if there is any change of this association over time. The aim of the present study was to assess the association between maternal GDM and offspring's adiposity risk from 6 to 8 years of age.

Materials and Methods

Study Design and Participants

The present study was a part of the Tianjin Gestational Diabetes Mellitus Prevention Program (TGDMPP) [15–17], and the study design, including recruitment, screening visits, and inclusion and exclusion criteria, has been described in detail elsewhere [8, 15–17]. Briefly, 76,325 pregnant women from six urban districts in Tianjin were screened at 26–30 gestational weeks between 2005 and 2009, among whom 4,644 women were diagnosed as GDM and 71,681 were free of GDM (Non-GDM). GDM was diagnosed on the basis of the 1999 World Health Organization (WHO) criteria [18] as either diabetes (fasting glucose ≥7.0 mmol/L or 2-hour glucose ≥11.1 mmol/L) or impaired glucose tolerance (2-hour glucose ≥7.8 mmol/L and <11.1 mmol/L). From August 2009 to July 2011, 1,263 of 4,644 GDM women participated in the TGDMPP, and then they were followed several times (Figure 1). We randomly chose 578 GDM mother–child pairs in the TGDMPP, who finished the second (Year 2) follow-up survey with stored blood samples, as the GDM case group. No differences at maternal age (32.3 compared with 32.4 years), BMI (23.9 compared with 24.0 kg/m^2), fasting glucose (5.21 compared with 5.23 mmol/L), and 2-h glucose (6.57 compared with 6.59 mmol/L) were found between GDM women selected and those not selected in the GDM case group. We simultaneously enrolled 578 non-GDM mother-child pairs from 71,681 non-GDM women who finished the GDM screening at the same period as the non-GDM control group, with children's age (±1 month) and sex frequency-matched to 578 children of GDM mothers. The 1,156 mother-child pairs (578 GDM and 578 non-GDM) finished the follow-up visit at 5.9±1.2 years postpartum. About 2 years later, 912 (486 GDM and 426 non-GDM) of 1,156 mother-child pairs finished another follow-up visit at 8.3±1.6 years postpartum. The flow chart of the participants was shown in Figure 1. This study was approved by the Ethics Committee for Clinical Research of Tianjin Women's and Children's Health Center (Approval numbers: 2009-01, 2013-03-01 and 2017-03-01), and written informed consents were collected from all participants. All methods were performed in accordance with the relevant guidelines and regulations.

Questionnaires and measurements

In the 5.9-year and 8.3-year surveys, every mother completed a self-administered questionnaire including socio-demographic characteristics (age, marital status, education, income, and occupation); family history of diabetes; pregnancy outcomes (pre-pregnancy weight, weight gain during pregnancy and number of children); lifestyle in the past year including smoking habits (non-smoking, former smoking, current smoking), passive smoking status and alcohol intake; and leisure-time physical activity (0 min/day, < 30 min/day, ≥30 min/day). Children's information was collected by another questionnaire completed by their mothers including children's general information, such as sex, birth date, age, birth weight, birth length, lactation (exclusive formula, mixed or exclusive breast), lactation duration, sleeping time (≤8 hours/day, 9–10 hours/day, ≥11 hours/day), screen watching time, and outdoor physical activity time. A validated food frequency questionnaire to measure the children's frequency and quantity of intake of 35 major food groups and beverages during the past year was collected from children's mothers. The performance of

the food frequency questionnaire has been validated in the China National Nutrition and Health Survey in 2002 [19].

Using the standardized protocol, all mother-child pairs underwent physical examinations including body weight (wearing light clothes) and height (without shoes) in the 5.9-year and 8.3-year surveys by specially trained doctors. Body weight was measured to the nearest 0.01 kg by using a digital scale (TCS-60, Tianjin Weighing Apparatus Co., China). Standing height was measured to the nearest 0.1 cm using a stadiometer (SZG-180, Shanghai Zhengdahengqi, China). Children's waist circumference was measured midway between the lower rib margin and the iliac crest, and the measurement was rounded to the nearest 0.1 cm. Children's body fat percentage was measured using a body composition analyzer (Inbody J-20, South Korea). Skinfold thickness at triceps, subscapular and suprailiac region was measured accurately to the nearest 0.5 mm by a trained investigator using a sebum thickness meter (Jianmin, Xindonghuateng, China).

BMI was obtained by dividing weight in kilograms by the square of height in meters. Children's Z scores of BMI for age were calculated according to the WHO age- and sex-specific growth reference (0 ~ 60 months [20] and 5 ~ 19 years old [21]). Childhood overweight was defined as BMI ≥ 85^{th} percentiles (Z score of BMI for age ≥1.035), and obesity was defined as BMI ≥95^{th} percentiles (Z score of BMI for age ≥1.645). According to the Third National Health and Nutrition Examination Survey (NHANES III) waist circumference criteria in children [22], central obesity was defined as waist circumference ≥the 90^{th} percentiles for age- and sex-specific distribution. According to the National Health and Nutrition Examination Survey (NHANES) IV [23], high body fat was defined as body fat ≥the 90^{th} percentiles for age- and sex-specific distribution. Since the reference normative values were available in children starting from 5 years old, we defined high body fat only among the children over 5 years old.

Statistical analysis

Demographic and lifestyle data of mothers and children were analyzed based on maternal GDM status. Continuous variables were presented as means (standard deviation, SD) and were compared between groups using *T*-test of independent samples. Categorical variables were presented as frequencies (percentages) and were compared using the Chi-square test. We established generalized linear models (GLMs) to analyze the β values and 95% confidential intervals (CIs) of GDM with childhood adiposity measurements and their changes from the 5.9-year to 8.3-year visit, and the adjusted means (standard error, SE) based on maternal GDM status were also listed. Logistic regression was used to estimate the odds ratios (ORs) and 95% CIs of indicators of childhood adiposity by maternal GDM status. This study was a longitudinal design in which the same dependent variables (childhood adiposity indicators) were repeatedly measured over time (5.9 and 8.3 years of age) for the same children, thus general linear models of repeated measures were conducted to investigate the effect of time and its interaction with maternal GDM on childhood adiposity indicators. We included two models in the analyses: 1) Multivariate analyses were adjusted for maternal information (age, gestational age, education, smoking status, alcohol drinking status, pre-pregnancy BMI, weight gain during pregnancy, and BMI),

and children's information (age, sex, birth weight, outdoor time, screening watching time, sleeping duration, dietary energy intake, dietary fiber intake and energy intake from fat) at the baseline (5.9-year) visit when comparing children's baseline obesity indicators by maternal GDM status; 2) When comparing children's obesity indicators at the follow-up (8.3-year) visit or changes in obesity indicators from 5.9-year to 8.3-year visit by maternal GDM status, we adjusted for above maternal and children's confounding factors at the baseline visit, and the corresponding adiposity indicators measured at the baseline visit.

The intention-to-treat analyses that included all participants were conducted in the present study. Missing values for children who did not finish the 8.3-year visit were not missing completely at random (Little's MCAR test: Chi-square = 309.17, $f = 202$, $P < 0.001$), and were imputed using expectation maximization algorithm (EM). EM is an iterative procedure that substitutes missing data with their most likely values according to the empirical mean and the variance-covariance matrix observed in the data [24] and is one of the most commonly used procedures to impute missing data. The per-protocol (PP) analyses were performed as the sensitivity analysis excluding participants who did not finish the 8.3-year visit.

All statistical analyses were performed with SPSS statistics V.25.0 for Windows software package (IBM) and R 4.0 (R Foundation for Statistical Computing, Vienna, Austria) software programs. Two-sided $P < 0.05$ was considered statistically significant.

Results

Maternal and children's characteristics at the 5.9-year and 8.3-year visits according to maternal GDM status are shown in Table 1. Mothers with GDM were older at delivery, had a higher pre-pregnancy BMI and BMI at the 5.9-year visit, less weight gain during pregnancy and less education, and were less likely to smoke and drink alcohol, as compared with mothers without GDM. At the 5.9-year visit, there were no differences of age (5.9 years old) and sex (boys counted 52%) between the two groups of children born to mothers with GDM and without GDM, but children of GDM mothers had higher birth weight, longer screen watching time, less sleeping time, higher percentage of energy intake from fat and less diet fiber intake than children of mothers without GDM. Children of GDM mothers were older, had less outdoor activity time and sleeping time than those of non-GDM mothers at the 8.3-year visit. The proportions of overweight, obesity, central obesity and high body fat were higher among children of GDM mothers than those of mothers without GDM at both 5.9-year and 8.3-year visits (all P values were < 0.05) (Table 1).

Base on the intention-to-treat analyses (Table 2), children born to mothers with GDM had higher mean values of adiposity indicators (waist circumference, body fat, subscapular skinfold and suprailiac skinfold) at 5.9 and 8.3 years of age, in comparison with those born to mothers without GDM. The effects (β values) of GDM on adiposity indicators except for the Z score of BMI for age were larger at the 8.3-year visit than those at the 5.9-year visit. There was a positive association of maternal GDM with changes of childhood adiposity indicators from the 5.9-year to 8.3-year visit, and the β values were significantly larger than zero: +0.10 (95% CI: 0.02-0.18) for z score of BMI for age, +1.46 (95% CI: 0.70-2.22)

cm for waist circumference, +1.78% (95% CI: 1.16%-2.40%) for body fat, +2.40 (95% CI: 1.78-3.01) mm for triceps skinfold, +1.59 (95% CI: 1.10-2.09) mm for subscapular skinfold, and +2.03 (95% CI: 1.35-2.71) mm for suprailiac skinfold, respectively. These results were similar to those in the per-protocol analyses.

The main effects of potential confounders and their interaction with time on childhood adiposity indicators from general linear models of repeated measures were shown in Table 3. Maternal GDM was significantly associated with childhood adiposity indicators, and this association became stronger with time (Table 2 and Table 3).

The associations of maternal GDM with indicators of childhood adiposity at the 5.9-year and 8.3-year visits were shown in Figure 2. After adjustment for potential confounding variables, maternal GDM was associated with higher risks of childhood overweight, obesity, central obesity and high body fat (OR 1.44, 95% CI: 1.03-2.01; OR 1.53, 95% CI: 1.02-2.29; OR 1.57, 95% CI: 1.00-2.44; and OR 1.41, 95% CI: 0.98-2.02, respectively) at 5.9 years of age. The independent association of maternal GDM with indicators of childhood adiposity became stronger at 8.3 years of age, with the multivariable-adjusted ORs at 1.93 (95% CI: 1.36-2.75), 1.94 (95% CI: 1.28-2.94), 1.73 (95% CI: 1.03-2.91), and 2.03 (95% CI: 1.39-2.98) for childhood overweight, obesity, central obesity and high body fat, respectively. The results from the per-protocol analyses were similar as shown in Supplementary Figure 1.

Discussion

The present study longitudinally followed 1,156 mother-child pairs at 5.9±1.2 years postpartum and retained 912 mother-child pairs at 8.3±1.6 years postpartum. The results indicated that maternal GDM was an independent risk factor of childhood overweight/obesity at both 5.9 and 8.3 years of age, and this significant and positive association became stronger among children at 8.3 years than those at 5.9 years of age.

Previous studies found conflicting results on the association between maternal GDM and childhood adiposity. Although three meta-analyses attempted to address the association between maternal GDM and offspring's overweight at different developmental stages [10–12], the conclusions were quite different. One meta-analysis reported that the association of maternal GDM with childhood overweight risk tended to attenuate with the growth of offspring, with the adjusted ORs as 1.35 (1.15-1.58), 1.12 (1.00-1.25) and 0.96 (0.71-1.31) in early, mid and late childhood, respectively [10]. The second meta-analysis indicated that maternal GDM was associated with offspring's overweight in the pubertal period but not in early and late childhood, with the unadjusted ORs of maternal GDM for offspring overweight risk as 1.03 (0.78-1.37), 0.96 (0.58-1.61) and 1.84 (1.20-2.83) in 2-4, 5-10, and ≥11 years of age, respectively [11]. The third meta-analysis demonstrated that offspring of mothers with GDM had a markedly increased risk of overweight and this association increased with age, with the adjusted ORs of maternal GDM for childhood overweight as 1.14 (1.06-1.22), 1.37 (1.31-1.44), 2.00 (1.79-2.23) and 2.05 (1.65-2.55) among children under 5 years, 5 to <10 years, 10 to <18 years, and over 18 years of age, respectively [12]. The inconsistent findings of these three meta-analyses may be partially due to

small sample sizes, especially GDM cases, and inadequate control for major confounders (maternal pre-pregnancy BMI, children's dietary intake, and physical activity, etc.) [10–12]. Besides, most of the original studies included in these three meta-analyses assessed the association of maternal GDM with offspring's overweight at a single age point, and very few studies assessed if there was any change of this association over time. The Environmental Determinants of Diabetes in the Young (TEDDY) study indicated that maternal GDM was associated with an increased risk of childhood overweight at 6 years of age but not from 3 months to 3 years of age [25]. However, the above positive association of maternal GDM with childhood overweight at 6 years of age became no longer significant after additional adjustment for maternal pre-pregnancy BMI [25]. The present study longitudinally followed 1,156 mother-child pairs from the 5.9-year to 8.3-year visit, and added evidence that children born to GDM mothers had an increased risk of being overweight/obesity in late childhood, and this increased risk became larger from 5.9 years of age to 8.3 years of age. All these findings were independent from several important confounding factors including maternal pre-pregnancy BMI, gestational weight gain, children's birth weight and lifestyle factors.

BMI has been widely used as a simple measure of defining obesity. However, it only reflects the general weight and cannot differentiate between fat mass and fat-free mass. It has been proven that waist circumference is a surrogate measure to estimate central adiposity. Body fat percent is a direct reflection of overall obesity, and skinfold thickness is conventionally used to classify an individual in terms of relative fat or to evaluate specific subcutaneous tissue fat [14]. Different from most previous studies that assessed the association between maternal GDM and childhood adiposity only using BMI as the indicator to evaluate obesity/overweight, the present study used BMI and other adiposity indicators including waist circumference, body fat percent and skinfolds to reflect obesity, and found that children born to mothers with GDM had higher mean values of adiposity indicators (Z score of BMI for age, waist circumference, body fat, and skinfolds) at 5.9 and 8.3 years of age, and larger mean values of changes in adiposity indicators from 5.9 to 8.3 years of age, in comparison with those born to mothers without GDM.

There are several underlying mechanisms that maternal GDM can increase the risk of offspring's adiposity, so our findings are biologically plausible. First, development in a diabetic intrauterine environment results in excess fetal growth. Maternal glucose but not maternal insulin can freely cross the placenta, so the developing fetal pancreas responds to this increased glucose load by producing additional insulin, which in turn acts as a fetal growth hormone promoting growth and adiposity [26]. Second, intrauterine exposure to GDM can also lead to epigenetic changes and impact the expression of genes that direct the accumulation of body fat or related metabolism [27].

There are several strengths of our study. First, we used BMI and other adiposity indicators including waist circumference, body fat percent and skinfolds to reflect general obesity, central obesity and adiposity, which would give a more comprehensive picture of obesity. Second, our study recruited a larger number of GDM and non-GDM mother-child pairs matched by children's age and sex, which were more powerful to explore the association between maternal GDM and the risk of childhood adiposity. Third, a variety of covariates

were controlled in the multivariable-adjusted analysis, including maternal social-economic characteristics, maternal gestational weight gain, pre-pregnancy BMI and current BMI, children's general characteristics, children's birth weight, diet and lifestyle, which were identified as important confounders of this association [28, 29]. Children of GDM mothers are more likely to be adiposity due to lifestyle differences between the groups, and the same lifestyle issues may also persist as a household issue. In the present study, we found that children born to GDM mothers had longer screen watching time, shorter sleeping duration, higher fat intake and less diet fiber intake, as compared with their counterparts. In our multivariate analyses, the association of maternal GDM with childhood adiposity risk at 6 and 8 years of age was independent from some confounding factors including maternal pre-pregnancy BMI, gestational weight gain, children's birth weight, lifestyle factors (outdoor time, screening watching time, sleeping duration, dietary energy intake, dietary fiber intake and energy intake from fat), and other related maternal and children's factors.

Our study also has limitations. First, this is an observational study where causality cannot be judged. Second, maternal GDM was diagnosed based on the 1999 WHO criteria, which were quite different from other criteria including the International Association of Diabetes and Pregnancy Study Group (IADPSG) criteria [30]. So the extensibility of this study may be affected. Finally, maternal pre-pregnancy weight and gestational weight gain were based on self-reported data, which might introduce recall bias. Nevertheless, validation studies in the United States and England have found good concordance between self-reported information during pregnancy and clinical records [31].

In conclusion, maternal GDM was an independent risk factor of childhood overweight/obesity, central obesity, and high body fat, which was independent from several important confounders including maternal pre-pregnancy BMI, gestational weight gain, children's birth weight and lifestyle factors at both 5.9 and 8.3 years of age. This significant and positive association became stronger with age. Therefore, children born to GDM mothers should be paid more attention by the health system, and it is critically important for this high-risk group of children to adopt an active lifestyle to reduce the burden of overweight in later life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding

This study was supported by grants from the European Foundation for the Study of Diabetes (EFSD)/Chinese Diabetes Society (CDS)/Lilly programme for Collaborative Research between China and Europe, and the National Institute of Diabetes and Digestive and Kidney Diseases (R01DK100790). Dr. Hu was partially supported by the grant from the National Institute of Diabetes and Digestive and Kidney Diseases (R01DK132011), the National Institute of General Medical Sciences (U54GM104940), and the Public University Partnership Program at the Louisiana Department of Health, Bureau of Health Services Financing.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Reference

1. Hu K, Staiano AE. Trends in Obesity Prevalence Among Children and Adolescents Aged 2 to 19 Years in the US From 2011 to 2020. JAMA Pediatr 2022; 176(10): 1037–1039. [PubMed: 35877133]
2. Collaboration NCDRF. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet 2017; 390(10113): 2627–2642. [PubMed: 29029897]
3. Weiss R, Kaufman FR. Metabolic complications of childhood obesity: identifying and mitigating the risk. Diabetes care 2008; 31 Suppl 2: S310–6. [PubMed: 18227502]
4. Singh AS, Mulder C, Twisk JW, van Mechelen W, Chinapaw MJ. Tracking of childhood overweight into adulthood: a systematic review of the literature. Obesity reviews : an official journal of the International Association for the Study of Obesity 2008; 9(5): 474–88. [PubMed: 18331423]
5. Wang H, Li N, Chivese T, Werfalli M, Sun H, Yuen L et al. IDF Diabetes Atlas: Estimation of Global and Regional Gestational Diabetes Mellitus Prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's Criteria. Diabetes research and clinical practice 2022; 183: 109050. [PubMed: 34883186]
6. Zhou T, Du S, Sun D, Li X, Heianza Y, Hu G et al. Prevalence and Trends in Gestational Diabetes Mellitus Among Women in the United States, 2006-2017: A Population-Based Study. Front Endocrinol (Lausanne) 2022; 13: 868094. [PubMed: 35733768]
7. Zhao P, Liu E, Qiao Y, Katzmarzyk PT, Chaput JP, Fogelholm M et al. Maternal gestational diabetes and childhood obesity at age 9-11: results of a multinational study. Diabetologia 2016; 59(11): 2339–48. [PubMed: 27510911]
8. Wang J, Wang L, Liu H, Zhang S, Leng J, Li W et al. Maternal Gestational Diabetes and Different Indicators of Childhood Obesity - A Large Study. Endocr Connect 2018; 7(2): 1464–1471. [PubMed: 30508416]
9. Wang J, Pan L, Liu EQ, Liu HY, Liu J, Wang ST et al. Gestational diabetes and offspring's growth from birth to 6 years old. Int J Obesity 2019; 43(4): 663–672.
10. Patro Golab B, Santos S, Voerman E, Lawlor DA, Jaddoe VWV, Gaillard R et al. Influence of maternal obesity on the association between common pregnancy complications and risk of childhood obesity: an individual participant data meta-analysis. Lancet Child Adolesc Health 2018; 2(11): 812–821. [PubMed: 30201470]
11. Kawasaki M, Arata N, Miyazaki C, Mori R, Kikuchi T, Ogawa Y et al. Obesity and abnormal glucose tolerance in offspring of diabetic mothers: A systematic review and meta-analysis. PloS one 2018; 13(1): e0190676. [PubMed: 29329330]
12. Gao M, Cao S, Li N, Liu J, Lyu Y, Li J et al. Risks of overweight in the offspring of women with gestational diabetes at different developmental stages: A meta-analysis with more than half a million offspring. Obesity reviews : an official journal of the International Association for the Study of Obesity 2022; 23(3): e13395. [PubMed: 34820996]
13. Wells JC. Toward body composition reference data for infants, children, and adolescents. Adv Nutr 2014; 5(3): 320S–9S. [PubMed: 24829484]
14. Dixit S, Gular K, Gautam AP, Reddy RS, Ahmad I, Tedla JS et al. Association between Handgrip Strength, Skinfold Thickness, and Trunk Strength among University Students. Diagnostics (Basel) 2023; 13(5).
15. Hu G, Tian H, Zhang F, Liu H, Zhang C, Zhang S et al. Tianjin Gestational Diabetes Mellitus Prevention Program: study design, methods, and 1-year interim report on the feasibility of lifestyle intervention program. Diabetes research and clinical practice 2012; 98(3): 508–17. [PubMed: 23010556]
16. Liu H, Wang L, Zhang S, Leng J, Li N, Li W et al. One-year weight losses in the Tianjin Gestational Diabetes Mellitus Prevention Programme: A randomized clinical trial. Diabetes Obes Metab 2018; 20(5): 1246–1255. [PubMed: 29360237]

17. Li W, Zhang S, Liu H, Wang L, Zhang C, Leng J et al. Different associations of diabetes with beta-cell dysfunction and insulin resistance among obese and nonobese Chinese women with prior gestational diabetes mellitus. Diabetes Care 2014; 37(9): 2533–9. [PubMed: 24914241]
18. WHO. WHO Consultation: Definition, Diagnosis and Classification of Diabetes mellitus and Its Complications. Part 1: Diagnosis and Classification of Diabetes mellitus. World Health Organisation; Geneva, Switzerland: 1999.
19. Li YP, He YN, Zhai FY, Yang XG, Hu XQ, WH Z et al. Comparison of assessment of food intakes by using 3 dietary survey methods. Chin J Prev Med 2006; 40: 273–79.
20. Group WHOMGRS. WHO Child Growth Standards based on length/height, weight and age. Acta Paediatr Suppl 2006; 450: 76–85. [PubMed: 16817681]
21. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. Bull World Health Organ 2007; 85(9): 660–7. [PubMed: 18026621]
22. Fernandez JR, Redden DT, Pietrobelli A, Allison DB. Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents. The Journal of pediatrics 2004; 145(4): 439–44. [PubMed: 15480363]
23. Laurson KR, Eisenmann JC, Welk GJ. Body fat percentile curves for U.S. children and adolescents. American journal of preventive medicine 2011; 41(4 Suppl 2): S87–92. [PubMed: 21961617]
24. Do CB, Batzoglou S. What is the expectation maximization algorithm? Nat Biotechnol 2008; 26(8): 897–9. [PubMed: 18688245]
25. Pitchika A, Vehik K, Hummel S, Norris JM, Uusitalo UM, Yang J et al. Associations of Maternal Diabetes During Pregnancy with Overweight in Offspring: Results from the Prospective TEDDY Study. Obesity (Silver Spring) 2018; 26(9): 1457–1466. [PubMed: 30226003]
26. Lu J, Gu Y, Wang L, Li W, Zhang S, Liu H et al. Glucose metabolism among obese and non-obese children of mothers with gestational diabetes. BMJ open diabetes research & care 2020; 8(1).
27. Slupecka-Ziemilska M, Wychowanski P, Puzianowska-Kuznicka M. Gestational Diabetes Mellitus Affects Offspring's Epigenome. Is There a Way to Reduce the Negative Consequences? Nutrients 2020; 12(9).
28. Li W, Wang L, Li N, Liu H, Zhang S, Hu G et al. Maternal Prepregnancy BMI and Glucose Level at 24-28 Gestational Weeks on Offspring's Overweight Status within 3 Years of Age. BioMed research international 2017; 2017: 7607210. [PubMed: 28251156]
29. Li N, Liu E, Guo J, Pan L, Li B, Wang P et al. Maternal prepregnancy body mass index and gestational weight gain on offspring overweight in early infancy. PloS one 2013; 8(10): e77809. [PubMed: 24204979]
30. Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes care 2010; 33(3): 676–82. [PubMed: 20190296]
31. Dietz P, Bombard J, Mulready-Ward C, Gauthier J, Sackoff J, Brozicevic P et al. Validation of self-reported maternal and infant health indicators in the Pregnancy Risk Assessment Monitoring System. Maternal and child health journal 2014; 18(10): 2489–98. [PubMed: 24770954]

Key Points

What is already known about this subject?

Previous studies found conflicting results on the association between maternal gestational diabetes mellitus (GDM) and childhood overweight/obesity, and most of them only used body mass index as the adiposity indicator, which cannot reflect body composition. Evidence from longitudinal studies to assess the association between maternal gestational diabetes mellitus (GDM) and childhood adiposity risk is still needed.

What are the new findings of this manuscript?

It added evidence that maternal GDM was a risk factor of childhood overweight/obesity, central obesity and high body fat at both 6 and 8 years of age, which was independent from several confounders such as maternal pre-pregnancy body mass index, gestational weight gain, children's birth weight and lifestyle factors. This significant and positive association became stronger with age.

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

Children of GDM mothers are facing an increasing risk of obesity with age, and appropriate intervention strategies are needed for this high-risk population.

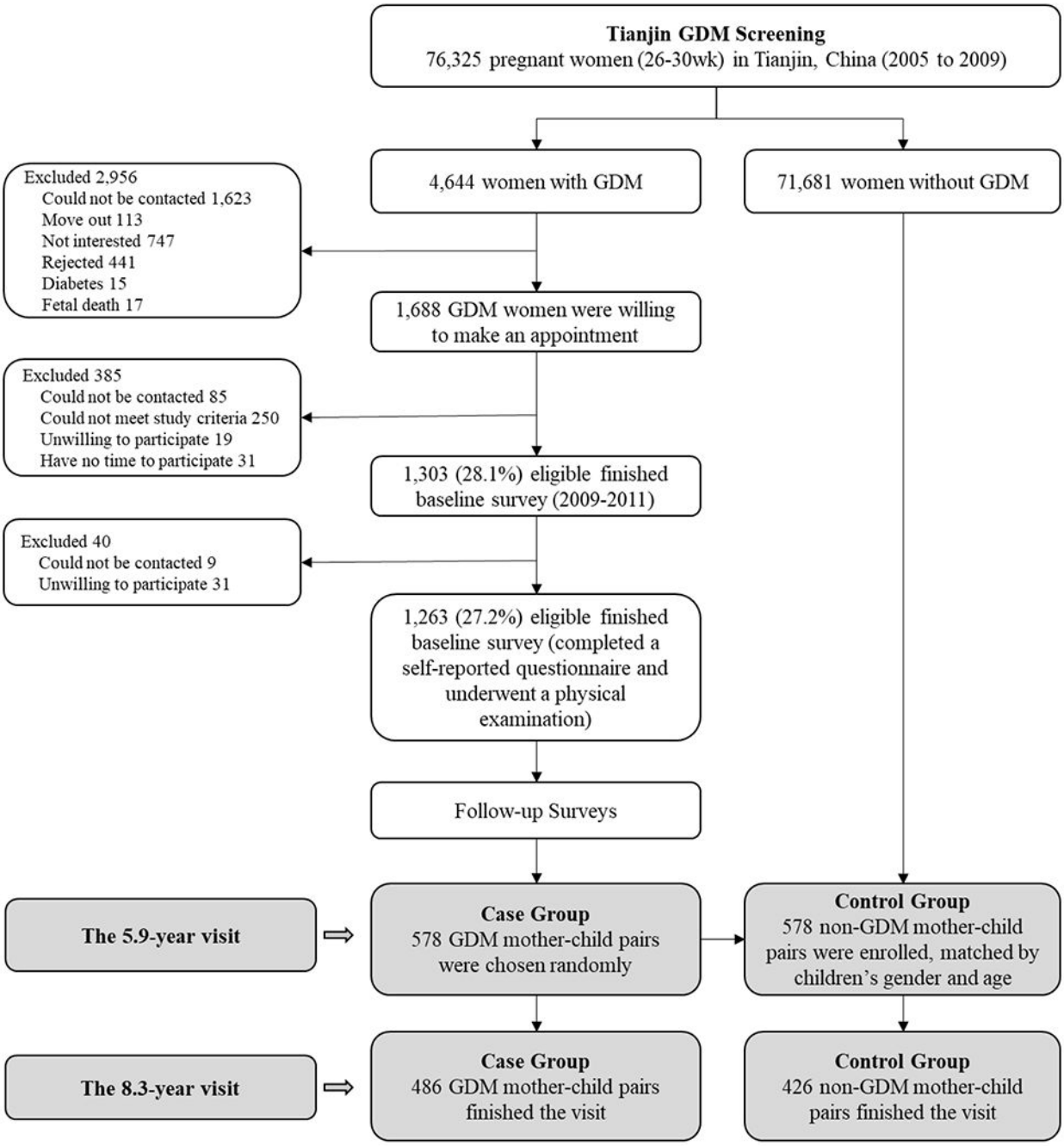

Figure 1.
Participant flow chart.

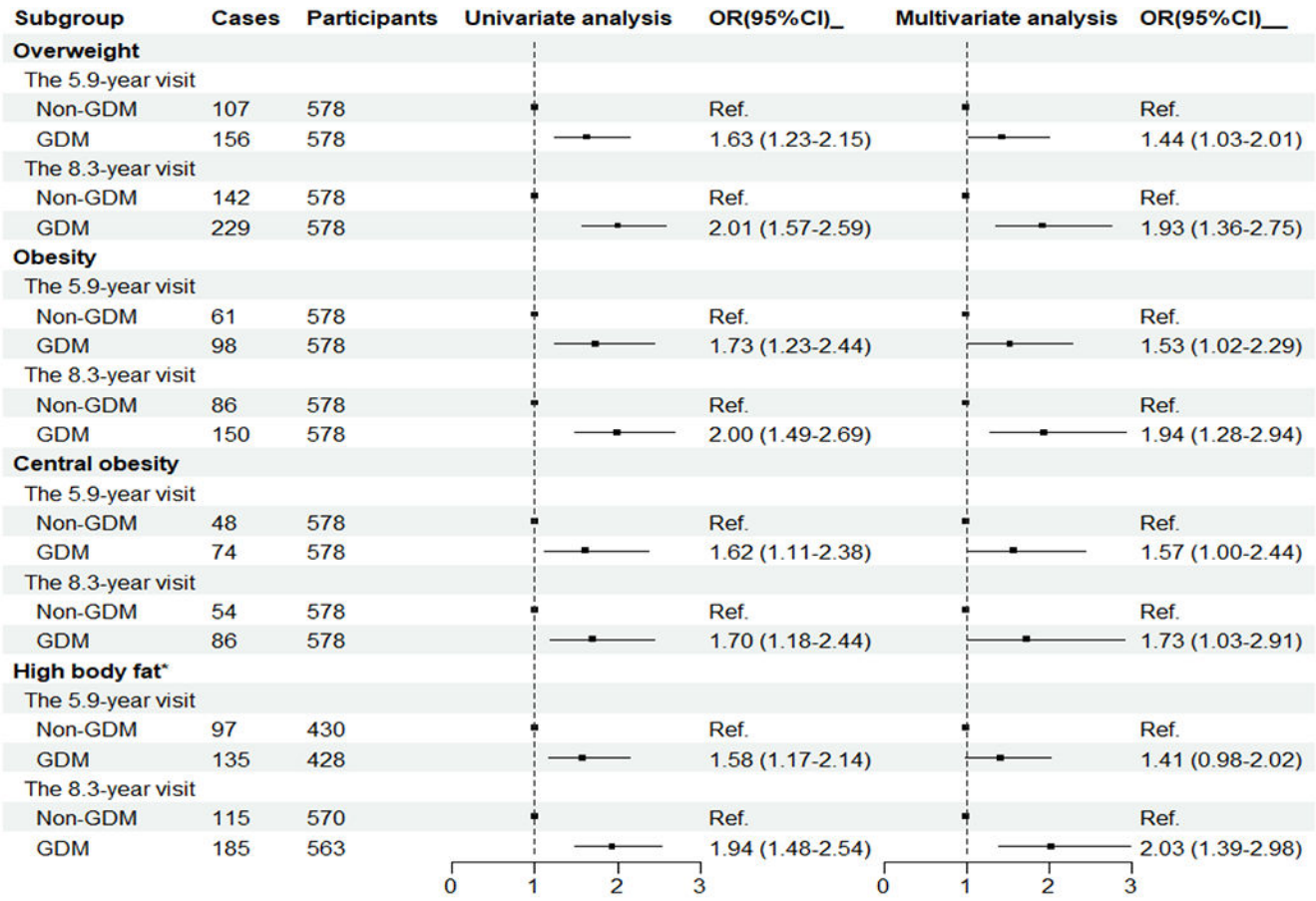

Figure 2.

Forest plot of odds ratios for the association of maternal gestational diabetes mellitus with indicators of childhood adiposity at the 5.9-year and 8.3-year visits based on the intention-to-treat analyses.

Notes: Intention-to-treat analyses, missing values for children who did not finish the 8.3-year visit were imputed using expectation maximization algorithm. Per-protocol analyses, excluding participants who did not finish the 8.3-year visit. *There were 298 and 23 children in the 5.9-year and 8.3-year visits respectively who were younger than 5 years old and not included since the references were available from 5 years old.

Abbreviations: GDM, gestational diabetes mellitus; OR, odds ratio; CI, confidence interval.

Table 1.

Maternal and children's characteristics according to maternal gestational diabetes status

	The 5.9-year visit			The 8.3-year visit		
	Non-GDM	**GDM**	***P* value**	**Non-GDM**	**GDM**	***P* value**
Number of subjects	578	578		578	578	
Maternal characteristics						
Age at delivery, years	30.5±2.91	31.2±3.58	<0.001	-	-	-
Gestational age at delivery, weeks	39.1±1.52	39.1±1.34	0.542	-	-	-
Pre-pregnancy BMI, kg/m^2	21.4±2.94	22.9±3.06	<0.001	-	-	-
Gestational weight gain, kg	18.3±6.70	16.6±5.85	<0.001	-	-	-
Education, n (%)			<0.001			
≤ 12 years	62 (10.7)	116 (20.1)		-	-	-
13-15 years	437 (75.6)	421 (72.8)		-	-	-
≥ 16 years	79 (13.7)	41 (7.1)		-	-	-
Current smokers, %	22 (3.8)	10 (1.7)	0.046	-	-	-
Passive smokers, %	317 (54.8)	305 (52.8)	0.480	-	-	-
Alcohol drinkers, %	183 (31.7)	125 (21.6)	<0.001	-	-	-
Maternal BMI at the 5.9-year visit, kg/m^2	22.8±3.60	24.0±3.67	<0.001			
Child characteristics						
Boy, %	302 (52.2)	302 (52.2)	1.000			
Age, years	5.87±1.23	5.87±1.24	0.980	7.90±1.55	8.67±1.63	<0.001
Birth weight, g	3401±454	3544±507	<0.001	-	-	-
Mode of infant feeding, %			0.420			
Exclusive breastfeeding	236 (40.8)	256 (44.3)		-	-	-
Mixed breast and formula	257 (44.5)	248 (42.9)		-	-	-
Exclusive formula feeding	85 (14.7)	74 (12.8)		-	-	-
Outdoor activity, hours/day	2.11±0.85	2.20±0.90	0.097	1.12±0.55	1.00±0.32	<0.001
Screen watching time, hours/day	0.95±0.76	1.17±0.83	<0.001	0.76±0.65	0.73±0.61	0.420
Sleeping duration, n (%)			<0.001			<0.001
≤ 8 hours/day	64 (11.1)	88 (15.2)		131 (30.7)	248 (51.0)	
9-10 hours/day	389 (67.3)	412 (71.3)		266 (62.3)	235 (48.4)	
≥ 11 hours/day	125 (21.6)	78 (13.5)		30 (7.0)	3 (0.6)	
Energy intake, kcal/day	1400±405	1390±465	0.680	-	-	-
Energy intake from fat, %	22.7±5.53	23.9±6.67	0.001	-	-	-
Diet fiber, grams/1000 kcal	5.46±1.31	5.20±1.29	0.001	-	-	-
Indicators of childhood adiposity						
Continuous variables						
Z score of BMI for age	0.02±1.28	0.34±1.35	<0.001	0.16±1.38	0.59±1.48	<0.001
Waist circumference (cm)	54.7±6.15	56.3±6.75	<0.001	59.0±8.17	62.9±9.76	<0.001
Body fat (%)	19.0±7.4	20.8±7.99	<0.001	20.5±8.48	24.5±9.55	<0.001
Triceps skinfold (mm)	12.8±5.36	12.7±5.81	0.689	15.2±6.69	18.0±7.87	<0.001
Subscapular skinfold (mm)	7.22±3.82	8.10±4.42	<0.001	9.19±5.56	11.9±7.32	<0.001

	The 5.9-year visit			The 8.3-year visit		
	Non-GDM	**GDM**	***P* value**	**Non-GDM**	**GDM**	***P* value**
Suprailiac skinfold (mm)	9.67±5.96	11.6±6.99	<0.001	13.2±7.90	17.4±9.90	<0.001
Categorical variables						
Overweight (Z score of BMI for age ≥1.035), %	107 (18.5)	156 (27.0)	0.001	142 (24.6)	229 (39.6)	<0.001
Obesity (Z score of BMI for age ≥1.645), %	61 (10.6)	98 (17.0)	0.002	86 (14.9)	150 (26.0)	<0.001
Central obesity, %	48 (8.3)	74 (12.8)	0.013	54 (9.3)	86 (14.9)	0.004
High body fat, %*	97 (22.6)	135 (31.5)	0.003	115 (20.2)	185 (32.9)	<0.001

Values shown are means ± SD or n (%). BMI, body mass index; GDM, gestational diabetes mellitus.

Missing values for children who did not finish the 8.3-year visit were imputed using expectation maximization algorithm.

*There were 298 and 23 children in the 5.9-year and 8.3-year visits, who were younger than 5 years old and not included since the references were available from 5 years old.

Table 2.

Comparison of children's baseline and follow-up measurements and their changes according to maternal gestational diabetes status

	Intention-to-treat analyses				Per-protocol analyses			
	Non-GDM*	GDM*	β values (95% CI)	*P* value	Non-GDM*	GDM*	β values (95% CI)	*P* value
Number of subjects	578	578	-	-	486	426	-	-
Z score of BMI for age								
The 5.9-year visit†	0.16 (0.12)	0.30 (0.12)	0.15 (0.00, 0.29)	0.049	0.25 (0.14)	0.41 (0.14)	0.16 (0.00, 0.32)	0.052
The 8.3-year visit‡	0.31 (0.09)	0.41 (0.09)	0.10 (−0.01, 0.21)	0.062	0.31 (0.09)	0.41 (0.09)	0.11 (0.00, 0.22)	0.057
Changes from 5.9-year to 8.3-year visit‡	0.12 (0.07)	0.22 (0.07)	0.10 (0.02, 0.18)	0.020	0.11 (0.09)	0.24 (0.09)	0.13 (0.02, 0.23)	0.018
Waist circumference (cm)								
The 5.9-year visit†	55.3 (0.55)	56.4 (0.56)	1.14 (0.49, 1.80)	0.001	55.5 (0.63)	56.7 (0.64)	1.12 (0.41, 1.84)	0.002
The 8.3-year visit‡	60.6 (0.66)	62.1 (0.66)	1.46 (0.70, 2.22)	<0.001	60.6 (0.66)	62.1 (0.66)	1.48 (0.71, 2.24)	<0.001
Changes from 5.9-year to 8.3-year visit‡	5.20 (0.66)	6.66 (0.66)	1.46 (0.70, 2.22)	<0.001	5.18 (0.66)	6.66 (0.66)	1.48 (0.71, 2.24)	<0.001
Body fat (%)								
The 5.9-year visit†	20.2 (0.73)	21.4 (0.75)	1.19 (0.31, 2.06)	0.008	20.5 (0.86)	21.8 (0.88)	1.25 (0.26, 2.23)	0.013
The 8.3-year visit‡	21.5 (0.67)	22.9 (0.67)	1.46 (0.68, 2.23)	<0.001	21.4 (0.67)	22.9 (0.67)	1.48 (0.70, 2.26)	<0.001
Changes from 5.9-year to 8.3-year visit‡	1.30 (0.52)	3.09 (0.53)	1.78 (1.16, 2.40)	<0.001	1.11 (0.68)	3.38 (0.69)	2.27 (1.50, 3.05)	<0.001
Triceps skinfold (mm)								
The 5.9-year visit†	13.8 (0.51)	13.3 (0.53)	−0.47 (−1.08, 0.15)	0.138	13.9 (0.59)	13.4 (0.60)	−0.59 (−1.26, 0.08)	0.085
The 8.3-year visit‡	14.8 (0.64)	16.8 (0.65)	2.04 (1.30, 2.79)	<0.001	14.7 (0.64)	16.8 (0.65)	2.07 (1.32, 2.81)	<0.001
Changes from 5.9-year to 8.3-year visit‡	1.93 (0.51)	4.33 (0.53)	2.40 (1.78, 3.01)	<0.001	1.70 (0.66)	4.63 (0.67)	2.93 (2.18, 3.68)	<0.001
Subscapular skinfold (mm)								
The 5.9-year visit†	7.67 (0.38)	8.23 (0.39)	0.56 (0.10, 1.02)	0.016	7.74 (0.44)	8.34 (0.44)	0.60 (0.10, 1.10)	0.018
The 8.3-year visit‡	10.0 (0.52)	11.2 (0.53)	1.23 (0.62, 1.84)	<0.001	9.98 (0.52)	11.2 (0.53)	1.25 (0.64, 1.86)	<0.001
Changes from 5.9-year to 8.3-year visit‡	2.06 (0.41)	3.65 (0.42)	1.59 (1.10, 2.09)	<0.001	1.90 (0.54)	3.88 (0.55)	1.98 (1.37, 2.59)	<0.001
Suprailiac skinfold (mm)								
The 5.9-year visit†	10.5 (0.60)	11.8 (0.61)	1.33 (0.61, 2.04)	<0.001	10.7 (0.68)	12.2 (0.69)	1.41 (0.64, 2.19)	<0.001
The 8.3-year visit‡	13.9 (0.57)	15.9 (0.58)	1.59 (1.10, 2.09)	<0.001	13.5 (0.74)	16.1 (0.75)	2.62 (1.77, 3.47)	<0.001

	Intention-to-treat analyses				Per-protocol analyses			
	Non-GDM*	**GDM***	**β values (95% CI)**	***P* value**	**Non-GDM***	**GDM***	**β values (95% CI)**	***P* value**
Changes from 5.9-year to 8.3-year visit‡	3.27 (0.57)	5.30 (0.58)	2.03 (1.35, 2.71)	<0.001	2.95 (0.74)	5.57 (0.75)	2.62 (1.77, 3.47)	<0.001

Intention-to-treat analyses, missing values for children who did not finish the 8.3-year visit were imputed using expectation maximization algorithm. Per-protocol analyses, excluding participants who did not finish the 8.3-year visit.

*Data shown are Means (SE).

†Adjusted for maternal information (age, gestational age, education, smoking status, alcohol drinking status, pre-pregnancy BMI, weight gain during pregnancy, and BMI), and children's information (age, sex, birth weight, outdoor time, screening watching time, sleeping duration, dietary energy intake, dietary fiber intake and energy intake from fat) at the baseline (5.9-year) visit.

‡Also adjusted for the corresponding adiposity indicators at the baseline visit in the analyses at the 8.3-year visit or changes from the 5.9-year to 8.3-year visit.

Table 3.

Main effect and within-subjects effects (time and its interaction with other factors) on childhood adiposity indicators from general linear models of repeated measures

	Z score of BMI for age		Waist circumference		Body fat		Triceps skinfold		Subscapular skinfold		Suprailiac skinfold	
	***F* value**	***P* value**	***F* value**	***P* value**	***F* value**	***P* value**	***F* value**	***P* value**	***F* value**	***P* value**	***F* value**	***P* value**
Tests of Between-Subjects Effects (main effects)												
GDM	6.46	0.011	31.5	<0.001	19.7	<0.001	5.93	0.015	24.9	<0.001	33.5	<0.001
Maternal pre-pregnancy BMI	15.5	<0.001	13.2	<0.001	7.64	0.006	3.48	0.062	5.42	0.020	9.79	0.002
Maternal gestational weight gain	15.4	<0.001	9.03	0.003	10.6	0.001	8.10	0.005	8.50	0.004	7.71	0.006
Maternal age at delivery	1.48	0.224	0.00	0.946	0.19	0.664	0.26	0.613	0.49	0.485	0.03	0.858
Maternal gestational age at delivery	7.56	0.006	6.41	0.011	6.95	0.008	7.04	0.008	1.92	0.166	6.72	0.010
Maternal education	1.99	0.137	1.71	0.182	1.91	0.148	0.51	0.602	1.99	0.137	1.14	0.321
Maternal current smoking	1.30	0.272	2.53	0.080	1.80	0.166	1.63	0.196	0.99	0.373	1.16	0.314
Maternal current alcohol drinking	0.94	0.332	1.69	0.194	0.51	0.474	1.42	0.234	0.28	0.596	0.76	0.385
Maternal BMI at 5.9-year visit	7.14	0.008	3.57	0.059	11.5	0.001	14.8	<0.001	8.29	0.004	7.51	0.006
Childhood age	0.06	0.807	141	<0.001	15.5	<0.001	79.3	<0.001	42.3	<0.001	57.5	<0.001
Childhood sex	7.35	0.007	8.40	0.004	9.45	0.002	5.15	0.023	6.38	0.012	6.89	0.009
Childhood birth weight	17.5	<0.001	6.40	0.012	3.09	0.079	2.44	0.118	0.03	0.868	0.96	0.329
Childhood outdoor activity	1.07	0.302	0.49	0.483	2.31	0.129	1.13	0.287	1.53	0.216	0.67	0.414
Childhood screen watching time	3.59	0.058	5.04	0.025	8.77	0.003	9.75	0.002	5.79	0.016	7.65	0.006
Childhood sleeping duration	2.61	0.074	1.71	0.181	1.29	0.277	1.29	0.276	1.91	0.148	2.93	0.054
Childhood energy intake	83.9	<0.001	130	<0.001	64.0	<0.001	87.0	<0.001	106	<0.001	93	<0.001
Childhood energy intake from fat	14.5	<0.001	16.9	<0.001	10.9	0.001	11.9	0.001	15.6	<0.001	13.9	<0.001
Childhood diet fiber	13.5	<0.001	9.45	0.002	12.1	0.001	9.97	0.002	10.6	0.001	10.9	0.001
Tests of Within-Subjects Contrasts												
Time	5.04	0.025	1.69	0.194	0.04	0.841	0.44	0.509	0.05	0.823	2.74	0.098
Time * GDM	3.71	0.054	33.8	<0.001	25.5	<0.001	59.8	<0.001	41.0	<0.001	30.7	<0.001
Time * Maternal pre-pregnancy BMI	0.07	0.786	0.07	0.794	3.10	0.078	1.92	0.166	0.04	0.834	0.06	0.801
Time * Maternal gestational weight gain	0.15	0.701	0.97	0.325	0.05	0.830	0.10	0.755	0.00	0.988	0.00	0.998
Time * Maternal age at delivery	0.02	0.900	0.26	0.613	2.00	0.157	0.19	0.660	1.62	0.204	1.24	0.265
Time * Maternal gestational age at delivery	5.66	0.018	3.07	0.080	2.67	0.102	3.00	0.084	1.86	0.172	7.34	0.007

	Z score of BMI for age		Waist circumference		Body fat		Triceps skinfold		Subscapular skinfold		Suprailiac skinfold	
	***F* value**	***P* value**	***F* value**	***P* value**	***F* value**	***P* value**	***F* value**	***P* value**	***F* value**	***P* value**	***F* value**	***P* value**
Time * Maternal education	1.77	0.170	6.39	0.002	5.23	0.005	5.21	0.006	2.98	0.051	2.78	0.062
Time * Maternal current smoking	0.55	0.579	0.99	0.373	0.00	0.999	0.48	0.620	0.30	0.738	0.17	0.847
Time * Maternal current alcohol drinking	1.19	0.275	0.60	0.439	4.79	0.029	4.28	0.039	0.25	0.614	2.33	0.127
Time * Maternal BMI at 5.9-year visit	2.58	0.108	2.50	0.114	0.25	0.616	0.30	0.586	2.91	0.088	1.77	0.184
Time * Childhood age	0.75	0.387	8.29	0.004	10.0	0.002	1.40	0.237	13.0	<0.001	4.16	0.042
Time * Childhood sex	10.68	0.001	5.63	0.018	7.09	0.008	5.69	0.017	1.75	0.186	9.90	0.002
Time * Childhood birth weight	0.10	0.757	3.25	0.072	0.67	0.414	1.11	0.293	0.15	0.695	0.21	0.645
Time * Childhood outdoor activity	0.91	0.341	0.07	0.789	1.04	0.308	0.94	0.332	0.08	0.772	0.01	0.927
Time * Childhood screen watching time	0.02	0.886	0.68	0.411	1.96	0.161	1.58	0.209	0.04	0.849	2.59	0.108
Time * Childhood sleeping duration	1.09	0.337	3.13	0.044	0.73	0.480	1.86	0.156	1.35	0.259	4.95	0.007
Time * Childhood energy intake	0.56	0.454	31.1	<0.001	9.95	0.002	28.5	<0.001	66.0	<0.001	47.0	<0.001
Time * Childhood energy intake from fat	6.32	0.012	9.89	0.002	7.54	0.006	1.07	0.301	3.41	0.065	6.25	0.013
Time * Childhood diet fiber	4.64	0.031	8.15	0.004	7.16	0.008	0.61	0.435	0.57	0.449	0.12	0.725

Results were based on intention-to-treat analyses. All *P*-values >0.05 for Mauchly's Test of Sphericity.