BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open: first published as 10.1136/bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open

The impact of Interpregnancy weight change on the risk of gestational diabetes mellitus during a second pregnancy in Chinese population：a retrospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-084282
Article Type:	Original research
Date Submitted by the Author:	14-Jan-2024
Complete List of Authors:	Yang, Ao; Peking University Shenzhen Hospital, Department of Obstetrics and Gynecology; Shenzhen PKU-HKUST Medical Center Wang, Ying; Peking University Shenzhen Hospital, Department of Obstetrics and Gynecology; Shenzhen PKU-HKUST Medical Center Liu, Yuzhen; Peking University Shenzhen Hospital, Department of Obstetrics and Gynecology; Shenzhen PKU-HKUST Medical Center Yang, Juan; Peking University Shenzhen Hospital, Department of Obstetrics and Gynecology; Shenzhen PKU-HKUST Medical Center Zhong, Shilin; Peking University Shenzhen Hospital, Department of Obstetrics and Gynecology; Shenzhen PKU-HKUST Medical Center
Keywords:	Diabetes in pregnancy < DIABETES & ENDOCRINOLOGY, OBSTETRICS, Weight Gain, Maternal medicine < OBSTETRICS, Risk Factors

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

The impact of Interpregnancy weight change on the risk of gestational diabetes mellitus during a second pregnancy in Chinese population：a retrospective cohort study

Ao Yang[1,2,3]*, Ying Wang[1,2,3]*, Yuzhen Liu[1,2,3]*, Juan Yang[1,2,3], Shilin Zhong[1,2,3]

[1]Department of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China.
[2]Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen, Guangdong, China.
[3]Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases, Shenzhen, Guangdong, China.
Ao Yang, Ying Wang and Yuzhen Liu contributed equally to this article.

Correspondence
Shilin Zhong, Department of Obstetrics and Gynecology, Peking University Shenzhen Hospital, 1120 Lianhua Road, Shenzhen 518036, Guangdong, China.
Email: zhongshilin2013@163.com

Abstract

Objectives This study aimed to investigate the impact of interpregnancy weight changes (IPWC) on the risk of gestational diabetes mellitus (GDM) in the second pregnancy.

Design A retrospective cohort study.

Setting Data were collected in Peking University Shenzhen Hospital from 2013 to 2021.

Participants Women who had two consecutive singleton deliveries after 28 gestational weeks (N=2372).

Outcomes The risk of GDM in the second pregnancy.

Methods: IPWC was divided into seven categories by units BMI (kg/m^2), with the range of -1 kg/m2 to 1 kg/m2 being used as the reference range. Adjusted odds ratios (aORs) with 95% CIs were obtained by multivariable logistic regression models to evaluate the association between interpregnancy BMI change on GDM. Analyses were stratified by interpregnancy interval (IPI), BMI and maternal age in the first pregnancy.

Results: IPWC⩾3 units was significantly associated with an increased risk of GDM in the second pregnancy, compared to the reference IPWC (aOR: 1.758, 95%CI: 1.149-2.688). No significant association was found between GDM risk and an IPWC increase of less than 3 units or any IPWC decrease (P>0.05). Unlike the overall study, stratified analysis revealed that significant association between GDM risk and IPWC ⩾ 3 units was only showed in participants with IPI ≤ 36 months(aOR: 2.165, 95%CI: 1.214-3.860), BMI ＞21kg/m^2(aOR: 2.256, 95%CI: 1.135-4.483) , or maternal age＞30 years(aOR: 2.381, 95%CI: 1.054-5.377) in the first pregnancy. There was no significant association between IPWC decline and GDM risk in any of the subgroups (P>0.05).

Conclusion: An increase in IPWC of 3 units or more may serve as a risk factor for GDM in the

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

second pregnancy, particularly among individuals with a shorter IPI, higher BMI, or older maternal age in the first pregnancy.

Keywords gestational diabetes mellitus, interpregnancy weight change, risk factor, maternal age, interpregnancy interval

Strength and limitations of this study

► The main limitation of our study is the retrospective design.
► The sample size for certain subgroups is relatively small.
► The data of diet, family history of diabetes, and gestational weight gain during the first pregnancy, were not included in the analysis.
► Confounding factors such as IPI, maternal age, GDM, HDCP, macrosomia, PTB, and cesarean section in the first pregnancy were adjusted in the multivariate logistic regression analysis.
► Analyses were stratified by interpregnancy interval, BMI and maternal age in the first pregnancy.

This study has several limitations. Firstly, it is a retrospective, single-center study, and all of the data were collected from historical databases. Some confounding factors, such as diet, family history of diabetes, and gestational weight gain during the first pregnancy, were not included in the analysis, which could potentially impact the results. Secondly, the sample size for certain subgroups, including individuals who are overweight or obese and those who experienced GDM in their first pregnancy with a BMI increase of three units or more, is relatively small. As a result, the statistical power in these subgroups is diminished. Thirdly, excluding 643 women who lacked the BMI information may have introduced selection bias.

INTRODUCTION

Gestational diabetes (GDM) is a type of diabetes that develops during pregnancy. In China, the prevalence of GDM is as high as 14.8%[1],leading to adverse consequences for both the mother and the fetus. Consequently, it is crucial to implement preventive actions to effectively manage the occurrence of diabetes in advance, yielding significant clinical relevance.

The occurrence of GDM is influenced by various factors, such as weight[2], diet[3], maternal age[4], exercise, and genetics[5]. Weight is particularly significant in relation to GDM development. Excessive weight gain during pregnancy proves to be a major risk factor for GDM[6,7]. Research conducted in China highlights the close relationship between pregestational weight and GDM[8].

A number of studies have suggested that there is a significant correlation between interpregnancy weight changes (IPWC) and GDM[9,10]. However, there is no consensus among current studies on how much an increase or decrease in BMI would significantly change the risk of GDM. Moreover, most current studies have not conducted stratified analysis according to interpregnancy interval (IPI) or maternal age. In addition, the study results are also different due to the difference in the study population, and the large sample study from the Chinese population is currently lacking.

Since 2016, China's two-child policy has been implemented to stimulate a rise in fertility levels. It has been found that 37% of couples have expressed intentions to have a second child[11].

For Peer Review Only
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

A higher proportion of advanced maternal age (>30 years) and multiparity have increased the risk of GDM[12]. The interpregnancy period is a critical time of health improvement and weight control to reduce the risk of GDM in a second pregnancy [13,14]. Regardless of whether they have had diabetes in their first pregnancy, both women and their physicians are interested in determining the ideal weight control target to minimize the risk of GDM in future pregnancies.

Therefore, we conducted a single-center, retrospective study in China to analyze the impact of weight change during two pregnancies on the risk of GDM in the second pregnancy. Our study indicates that a BMI increase of 3 units or more may be significantly linked to the risk of GDM in the Chinese population. These findings may offer guidance for weight management objectives.

MATERIALS ADN METHODS

Study design and Population

We conducted a retrospective cohort study on participants who had two consecutive single deliveries after 28 weeks at Peking University Shenzhen Hospital from 2013 to 2021. Exclusion criteria for this study included women who had multiple pregnancies, women with a parity of one, women with a parity of three or more, women who delivered before 28 gestational weeks, women without available BMI data, women with type 1 or type 2 diabetes, and women with unknown or unstated BMI for their first or second pregnancy. The study protocol was approved by the Medical Ethics Committee of Peking University Shenzhen Hospital (#2023-103). The participants were classified into two groups based on whether their second pregnancy was complicated by GDM: the GDM group and the non-GDM group.

Exposure and outcome

The main exposure of this study was interpregnancy weight change (IPWC), which is defined as the difference between the body mass index (BMI) in the first trimester of the second pregnancy and the BMI in the first trimester of the first pregnancy. IPWC is measured in units of BMI (kg/m^2) and was divided into seven categories: $\leqslant$-3kg/m^2, -3 kg/m^2 to <-2 kg/m^2, -2 kg/m^2 to <-1 kg/m^2, -1 kg/m^2 to <1 kg/m^2 (stable BMI, used as reference), 1 kg/m^2 to <2 kg/m^2, 2 kg/m^2 to <3 kg/m^2 and $\geqslant$3 kg/m^2. Individuals were categorized into four groups based on their BMI: underweight (<18.5 kg/m^2), normal weight (18.5 kg/m^2 to <24.0 kg/m^2), overweight or obese ($\geqslant$ 24.0 kg/m^2).The interpregnancy interval (IPI) was calculated by subtracting the gestational months of the second pregnancy from the total months between the two pregnancies.

The primary outcome of the study was the presence of GDM in the second pregnancy. Throughout the entire study period, GDM was diagnosed using the IADPSG criteria[15], which involved a 75-gram oral glucose tolerance test. According to these criteria, a diagnosis of GDM was made if the serum blood glucose levels were $\geqslant$5.1 mmol/L at 0 hours, and/or $\geqslant$10.0 mmol/L at 1 hour, and/or $\geqslant$10.0 mmol/L at 2 hours, between 24-28 weeks of gestation.

Data collection

The data for this study were obtained from the delivery records within the hospital information system. The collected variables include: IPI, maternal age, BMI, parity, year of delivery, delivery mode, occupation, medical payment method, ethnicity, marital status, sex of

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

newborn, birth weight, BMI during the first and second pregnancies, and the occurrence of GDM, thyroid disease, hypertensive disorder complicating pregnancy (HDCP), and preterm birth.

The study compared several variables between two groups, including the IPWC, IPI, maternal age at first pregnancy, birth weight of the first pregnancy newborn, BMI in the first and second pregnancy, and the occurrence of specific complications. Multivariate logistic regression was performed to identify independent risk factors for GDM in the second pregnancy. Furthermore, stratified analysis was conducted to assess the impact of IPWC on GDM risk in specific subgroups stratified based on IPI, BMI and maternal age in the first pregnancy. In stratified analysis, we estimated the minimum sample size required for each subgroup with an EPV of 10[16]. This estimation was based on the proportion of GDM occurrence and the number of independent variables included in the multivariate Logistic regression model. If the actual sample size in the initial stratification is smaller than the estimated minimum sample size, we will adjust the cut-off value of the stratification index to ensure that each subgroup meets the statistical requirements.

Statistical Analysis

The data analysis was performed using SPSS 24.0 statistical software (IBM, Armonk, NY, USA). Categorical variables were presented as n (%) and compared using the Chi-square test. Normally distributed variables were presented as mean ± standard deviation and compared using the student's *t*-test. Non-normally distributed variables were presented as median (interquartile range; IQR) and compared using the Mann-Whitney *U* test. Multivariable logistic regression models were used to assess the association between the independent variable (IPWC) and the risk of GDM in the second pregnancy, adjusting for maternal age, BMI, delivery mode, and other complications such as GDM and hypertension. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 35,675 participants who had experienced at least one pregnancy at Peking University Shenzhen Hospital were recorded between January 2013 and February 2021. After disqualifying 33,303 participants based on the exclusion criteria, a final cohort of 2,372 participants who had undergone two consecutive single deliveries were included (Figure 1).

In the first pregnancy, 534 cases (22.51%) were classified as underweight, 1620 cases (68.30%) as normal weight, and 218 cases (9.19%) as overweight or obese. In the second pregnancy, 371 cases (15.64%) were underweight, 1620 cases (68.30%) were normal weight, and 381 cases (16.06%) were overweight or obese. Of the 534 individuals who were underweight in their first pregnancy, approximately 49.25% of them maintained their initial pregnancy weight during their second pregnancy. This percentage decreased to 46.30% and 42.20% for the 1,620 individuals who were of normal weight and the 218 individuals who were overweight, respectively. Among those who were overweight in their first pregnancy, 46.25% experienced weight gain (IPWC > 1kg/m^2) during their second pregnancy. In comparison, the percentages for normal-weight, overweight, and obese individuals were 41.17%, and 29.82% respectively (Figure 2).

In the first pregnancy, a total of 265 cases (11.17%) developed GDM. 8.61% (46/534), 10.19% (165/1620), and 24.77% (54/218) of the underweight, normal weight, and overweight or obese groups participants, respectively, were complicated with GDM. In the second pregnancy,

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

303 cases (12.77%) were diagnosed with GDM. 7.55% (28/371), 11.98% (194/1620), and 21.26% (81/381) of the underweight, normal weight, and overweight or obese groups participants, respectively, were complicated with GDM.

In the GDM group, the maternal age, BMI, IPWC, and IPI (in months) were all significantly higher compared to the non-GDM group ($P < 0.01$, Table 1). Additionally, there was a greater proportion of GDM cases and CS deliveries in the GDM group when compared with the non-GDM group ($P < 0.01$, Table 1).

After adjusting for potential confounding factors such as IPI, maternal age, proportion of cases with GDM, HDCP, macrosomia, PTB, and cesarean section in the first pregnancy, our multivariate logistic regression analysis revealed that IPWC $\geqslant 3$ kg/m^2 was independently associated with an increased risk of GDM in the second pregnancy as compared to the reference IPWC ($P < 0.01$). However, there was no significant association between GDM risk and an IPWC increase of less than 3 kg/m^2 or any IPWC decrease ($P>0.05$). Additionally, we observed that IPI, maternal age, and GDM were also significantly associated with an increased GDM risk in the second pregnancy ($P < 0.01$) (Table 2).

In the analysis of stratification, we first divided the groups using an IPI of 36 months as the cut-off value. The proportion of GDM in the subgroup with an IPI$\leqslant$36 months was 10.59% (151 of 1426), while the proportion of GDM in the subgroup with an IPI>36 months was 16.07% (152 of 946). To correct for the 8 factors using the logistic binary regression model, a sample size of 756 and 498 was required for each subgroup, respectively, with an events per variable (EPV) of 10. Therefore, the sample size for the stratified analysis using an IPI of 36 months as the cut-off is sufficient.

Next, we categorized the subgroups into underweight, normal weight, and overweight or obese based on the BMI of the first pregnancy. The GDM proportion for these subgroups were 8.61% (46 of 534), 10.19% (165 of 1620), and 24.77% (54 of 218), respectively. The required sample sizes for these subgroups were 925, 785, and 323, respectively. Therefore, the sample size for this grouping is insufficient. To address this, we reduced the number of subgroups from 3 to 2 and calculated whether the sample size was sufficient for different BMI cut-off values, namely 24kg/m^2, 23kg/m^2, 22kg/m^2, and 21kg/m^2. Only when the BMI cut-off value was equal to 21kg/m^2 could we guarantee a sufficient sample size for both subgroups.

Similarly, when considering the cut-off value of 35 years old for the first pregnancy, the subgroup of advanced pregnancies did not have enough sample size. To address this issue, we adjusted the cut-off value to 30 years old, and both subgroups were able to obtain enough sample size.

Finally, in stratified analyses, we found significant associations between an increase of 3 units or more in IPWC and the risk of GDM in the second pregnancy among participants with IPI less than or equal to 36 months, BMI greater than 21kg/m^2, or maternal age greater than 30 years in the first pregnancy. However, no association was observed between an increase in IPWC and the risk of GDM in participants with IPI greater than 36 months, BMI less than or equal to 21kg/m^2, or maternal age less than or equal to 30 years in the first pregnancy. Additionally, we found no association between IPWC decline and GDM risk in any of the subgroups, which is consistent with the overall study findings (Table 3).

DISCUSSION

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

This study, conducted at a single center in China, suggests a significant association between the risk of GDM in the second pregnancy and a BMI increase of at least 3 units. In stratified analyses, we verified this finding among participants with IPI less than or equal to 36 months, BMI greater than 21kg/m^2, or maternal age greater than 30 years in the first pregnancy. Therefore, for women who want to avoid developing GDM in their second pregnancy, this study provides guidance on setting weight management goals. However, we did not find such an association between IPWC $\geqslant$3kg/m^2 and GDM risk in participants with IPI greater than 36 months, BMI less than or equal to 21kg/m^2, or maternal age less than or equal to 30 years in the first pregnancy. In addition, no association was found between GDM risk and a BMI increase of less than 3 units or a decrease in BMI.

Being overweight or obese prior to pregnancy is a significant risk factor for GDM[8]. Insulin resistance plays a crucial role in the development of GDM among individuals who are overweight[17]. Furthermore, excessive gestational weight gain (GWG) is closely linked to the occurrence of GDM[7,8].To mitigate the risk of GDM and macrosomia, the Institute of Medicine (IOM) suggests adopting appropriate GWG guidelines for single pregnancies based on pre-pregnancy weights[18]. Moreover, substantial weight gain before pregnancy has also been found to be associated with GDM[19].

Over the past decade, several studies conducted in different countries have suggested a potential link between interpregnancy weight change (IPWC) and the risk of GDM[9,10]. Whiteman et al.'s study identified a significant association between changes in BMI classification, particularly from normal to overweight or obese, and the risk of GDM[20]. Participants who experienced an increase in BMI had higher odds of developing GDM compared to those whose BMI remained unchanged[21].

The magnitude of BMI changes was also thought to be associated with GDM risk. Earlier investigations suggested that an increase of 3 or more units in BMI substantially increased the likelihood of developing GDM[22]. Subsequent research by Bogaerts et al[23]. and Knight-Agarwal et al[24]. also confirmed this finding, which is consistent with the results in our study. However, additional studies have suggested that even an increase of one or more units in BMI is associated with an increased risk of GDM[10, 25-29]. It is worth noting that there may be differences in the results of these studies due to factors such as varied diagnostic criteria or confounding factors adjusted for GDM. Unlike Sorbye et al. 's study[26], our study took into account confounding factors such as hypertensive disorders during pregnancy, macrosomia, preterm delivery, and cesarean section. Lynes et al.'s study [27] did not specify the diagnostic criteria used for GDM. Furthermore, Ehrlich et al. [25]reported that 94% of their 22,351 cases utilized the "two-step method" for diagnosing GDM, which differs from the method employed in our study. It is also important to consider that the results of these studies may vary across different study groups. The findings from our study, which was conducted in the Chinese population, complement those of previous studies that have primarily focused on populations in developed countries.

Unlike the overall study results, the results of stratified analysis suggests that the impact of IPWC on GDM varies in different populations. Even with a similar increase in BMI of three units or more, the risk of GDM differs based on IPI, maternal age, or BMI in the first pregnancy. Stratified analysis revealed that an increase in BMI of three units or more had a more significant impact on the risk of GDM in participants with a shorter IPI compared to those with a longer IPI. Compared to an interval of 24 to 35 months, an interval $\geqslant$36 months was associated with a higher risk of weight gain from the first to the second pregnancy[30]. Previous studies have also shown

For peer review only
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

that women with GDM tend to gain weight faster before pregnancy compared to non-GDM women[31]. Therefore, it would be more reasonable to investigate the association between weight change and GDM within a narrower range of IPI[23]. Tano et al. 's study suggested that annual BMI gain was associated with the risk of GDM during the subsequent pregnancy[32]. These studies imply that the risk of GDM is not only associated with increased BMI units but also with the rate at which BMI increases by three units or more. The effect of IPI on GDM risk diminishes after 36 months between pregnancies.

In similar studies, a cut-off value of 35 years was commonly used for age stratification. However, due to limited participant numbers, our study was unable to examine this association among women aged 35 years and older during their first pregnancy. Therefore, we adjusted the cut-off value for age stratification to 30 years. Consequently, our study revealed a significant association between an IPWC $\geqslant$ 3 units and an increased risk of GDM in women aged 30 years or older. This finding has important implications in establishing weight control goals based on age. Regrettably, no other stratified studies based on maternal age were identified in the existing literature. A study conducted in China found that women over the age of 30 had a higher risk of GDM compared to women aged 25-29[33]. Additionally, the risk of GDM in Asian women was more strongly correlated with age starting at 25 years old, compared to Europid women[34]. Based on these findings, it is possible that IPWC is significantly associated with the risk of GDM in Chinese women over the age of 35 during a second pregnancy. To further validate this hypothesis, further research with a larger sample size is necessary.

Due to the small sample size for pregnancies with overweight or obesity, we were unable to conduct multivariate stratified analysis on this population. However, when we adjusted the BMI cut-off to 21kg/m^2, we found that an increase of 3 units or more in IPWC was significantly associated with a higher risk of GDM in the higher BMI group. Conversely, there was no association between IPWC and GDM in the lower BMI group. These findings suggest that an increase of 3 units or more in IPWC should also be significantly associated with GDM risk in overweight or obese individuals (BMI greater than 24kg/m^2). In a study conducted by McBain et al., they suggested that an IPWC $\geqslant$2 units significantly increased the risk of GDM in overweight or obese groups, while an IPWC greater than 4 units was significantly associated with GDM risk in normal-weight groups [6]. This conclusion is consistent with the results of a study by Ku et al., who used IPWC $\pm$ 1 unit as a reference. In their study, an IPWC $\geqslant$ 1 unit significantly increased the risk of GDM in the subgroup with a BMI greater than 23 kg/m^2, while an IPWC $\geqslant$ 3 units increased the risk of GDM in the subgroup with a BMI less than 23 kg/m^2 [29]. Taken together, the results of these studies suggest that the risk of developing GDM in overweight or obese women is more influenced by IPWC than in women of normal weight. However, a systematic analysis by Martinez-Hortelano et al. suggests that an increase of 1 unit or more in IPWC is significantly associated with the risk of GDM, regardless of whether the BMI of the first pregnancy is greater than 25 kg/m^2 [28]. Additionally, Black et al. found that in obese or overweight women with GDM in their first pregnancy, only an IPWC $\geqslant$4 units significantly increased the risk of GDM in the second pregnancy compared to stable IPWC. On the other hand, in women without GDM (regardless of BMI value), an IPWC $\geqslant$ 1 unit significantly increased the risk of GDM[35]. This suggests that whether or not the initial pregnancy is accompanied by GDM may also influence the association between IPWC and the risk of GDM in a subsequent pregnancy.

Our study did not find evidence to support the protective effect of weight loss on GDM,

For peer review only
Enseignement Superieur (ABES) .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

which is consistent with the findings of other studies[24,26,27,29]. Three systematic analyses also yielded consistent results[9,36,37]. However, Martinez-Hortelano et al.'s stratified analyses suggest a decline in initial pre-pregnancy weight significantly reduced the risk of GDM in women with a body mass index (BMI) greater than 25kg/m^2 during their first pregnancy. This effect was not observed in women with a BMI less than 25kg/m^2 [28]. Conversely, a systematic analysis by Kirkegaard et al. found the opposite association: in women with a BMI less than 25 kg/m^2, a decrease in BMI was significantly associated with increased GDM risk[38]. Interestingly, Black et al.'s study found that for underweight or normal weight women with GDM in their first pregnancy, a decrease in BMI significantly increased the risk of GDM in a second pregnancy by 31% compared to maintaining a stable BMI [35]. These studies reveal ongoing uncertainty regarding the association between weight loss and GDM risk in different participant populations.

This study has several limitations. Firstly, it is a retrospective, single-center study, and all of the data were collected from historical databases. Some confounding factors, such as diet, family history of diabetes, and gestational weight gain during the first pregnancy, were not included in the analysis, which could potentially impact the results. Secondly, the sample size for certain subgroups, including individuals who are overweight or obese and those who experienced GDM in their first pregnancy with a BMI increase of three units or more, is relatively small. As a result, the statistical power in these subgroups is diminished. Thirdly, excluding 643 women who lacked the BMI information may have introduced selection bias.

CONCLUSION

Our study conducted in China revealed a noteworthy link between the risk of GDM during the second pregnancy and an increase of more than 3 units in BMI between two pregnancies. This finding was particularly observed in women with an interpregnancy interval (IPI) of 36 months or longer, normal weight, or a maternal age of 30 years or older during their first pregnancy. Furthermore, our study did not identify any correlation between the risk of GDM and a decline in IPWC. However, to obtain a more conclusive result, it is imperative to conduct further research with a larger sample size, focusing on the overweight or obese group, as well as the GDM subgroup.

Acknowledgments The authors thank all the participants in this study

Contributors SZ designed the study, supervised the work, reviewed and edited the manuscript. AY, YW, YL and JY collected the clinical data. AY, YW and YL researched the data, performed the statistical analysis and wrote the manuscript. All authors have read and approved the final manuscript.

Funding This study was granted by the Shenzhen Science and Technology Innovation Program (JCYJ20210324110206017) and the research project of Peking University Shenzhen Hospital (LCYJ2021010).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study protocol was approved by the Medical Ethics Committee of Peking

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

University Shenzhen Hospital (#2023-103).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

References

[1] Gao C, Sun X, Lu L, et al. Prevalence of gestational diabetes mellitus in mainland China: A systematic review and meta-analysis. J Diabetes Investig, 2019, 10(1):154-162.

[2] Goldstein RF, Abell SK, Ranasinha S, et al. Gestational weight gain across continents and ethnicity: systematic review and meta-analysis of maternal and infant outcomes in more than one million women. BMC Med, 2018, 16(1):153.

[3] Yamamoto JM, Kellett JE, Balsells M, et al. Gestational Diabetes Mellitus and Diet: A Systematic Review and Meta-analysis of Randomized Controlled Trials Examining the Impact of Modified Dietary Interventions on Maternal Glucose Control and Neonatal Birth Weight. Diabetes Care, 2018, 41(7):1346-1361.

[4] Zhang Y, Xiao CM, Zhang Y, et al. Factors Associated with Gestational Diabetes Mellitus: A Meta-Analysis. J Diabetes Res, 2021, 2021:6692695.

[5] Wu L, Cui L, Tam WH, et al. Genetic variants associated with gestational diabetes mellitus: a meta-analysis and subgroup analysis. Sci Rep, 2016, 6:30539.

[6] McBain RD, Dekker GA, Clifton VL, et al. Impact of inter-pregnancy BMI change on perinatal outcomes: a retrospective cohort study. Eur J Obstet Gynecol Reprod Biol, 2016, 205:98-104.

[7] Peng Y, Han N, Su T, et al. Gestational weight gain and the risk of gestational diabetes mellitus: A latent class trajectory analysis using birth cohort data. Diabetes Res Clin Pract, 2021, 182:109130.

[8] Sun Y, Shen Z, Zhan Y, et al. Effects of pre-pregnancy body mass index and gestational weight gain on maternal and infant complications. BMC Pregnancy Childbirth, 2020, 20(1):390.

[9] Oteng-Ntim E, Mononen S, Sawicki O, et al. Interpregnancy weight change and adverse pregnancy outcomes: a systematic review and meta-analysis. BMJ Open, 2018, 8(6):e018778.

[10] Nagpal TS, Souza SCS, Moffat M, et a;. Does prepregnancy weight change have an effect on subsequent pregnancy health outcomes? A systematic review and meta-analysis. Obes Rev, 2022, 23(1):e13324.

[11] Yang Y, He R, Zhang N, et al. Second-Child Fertility Intentions among Urban Women in China: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health, 2023, 20(4):3744.

[12] Zhu H, Zhao Z, Xu J, et al. The prevalence of gestational diabetes mellitus before and after the implementation of the universal two-child policy in China. Front Endocrinol (Lausanne), 2022, 13:960877.

[13] Wastnedge EAN, Fretwell J, Johns EC, et al. First and second pregnancy outcomes in women with class III obesity: An observational cohort study. Obes Res Clin Pract, 2021, 15(4):357-361.

[14] Liu J, Song G, Meng T, et al. Weight retention at six weeks postpartum and the risk of gestational diabetes mellitus in a second pregnancy. BMC Pregnancy Childbirth, 2019, 19(1):272.

[15] He Y, Ma RCW, McIntyre HD, et al. Comparing IADPSG and NICE Diagnostic Criteria for

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

GDM in Predicting Adverse Pregnancy Outcomes. Diabetes Care, 2022, 45(9):2046-2054.
[16] Wynants L, Bouwmeester W, Moons KG, et al. A simulation study of sample size demonstrated the importance of the number of events per variable to develop prediction models in clustered data. J Clin Epidemiol, 2015, 68(12):1406-1414.
[17] Zhu Y, Hedderson MM, Quesenberry CP, et al. Central Obesity Increases the Risk of Gestational Diabetes Partially Through Increasing Insulin Resistance. Obesity (Silver Spring), 2019, 27(1):152-160.
[18] Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines. Weight Gain During Pregnancy: Reexamining the Guidelines. Rasmussen KM, Yaktine AL, editors. Washington (DC): National Academies Press (US); 2009.
[19] Diouf I, Charles MA, Thiebaugeorges O, et al. Maternal weight change before pregnancy in relation to birthweight and risks of adverse pregnancy outcomes. Eur J Epidemiol, 2011, 26(10):789-796.
[20] Whiteman VE, Aliyu MH, August EM, et al. Changes in prepregnancy body mass index between pregnancies and risk of gestational and type 2 diabetes. Arch Gynecol Obstet, 2011, 284(1):235-240.
[21] Bender W, Hirshberg A, Levine LD. Interpregnancy Body Mass Index Changes: Distribution and Impact on Adverse Pregnancy Outcomes in the Subsequent Pregnancy. Am J Perinatol, 2019, 36(5):517-521.
[22] Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. Lancet, 2006, 368(9542):1164-1170.
[23] Bogaerts A, Van den Bergh BRH, Ameye L, et al. Interpregnancy weight change and risk for adverse perinatal outcome. Obstet Gynecol, 2013, 122(5):999-1009.
[24] Knight-Agarwal CR, Williams LT, Davis D, et al. Association of BMI and interpregnancy BMI change with birth outcomes in an Australian obstetric population: a retrospective cohort study. BMJ Open, 2016, 6(5):e010667.
[25] Ehrlich SF, Hedderson MM, Feng J, et al. Change in body mass index between pregnancies and the risk of gestational diabetes in a second pregnancy. Obstet Gynecol, 2011, 117(6):1323-1330.
[26] Sorbye LM, Skjaerven R, Klungsoyr K, et al. Gestational diabetes mellitus and interpregnancy weight change: A population-based cohort study. PLoS Med, 2017, 14(8):e1002367.
[27] Lynes C, McLain AC, Yeung EH, et al. Interpregnancy weight change and adverse maternal outcomes: a retrospective cohort study. Ann Epidemiol, 2017, 27(10):632-637.e5.
[28] Martínez-Hortelano JA, Cavero-Redondo I, Álvarez-Bueno C, et al. Interpregnancy Weight Change and Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis. Obesity (Silver Spring), 2021, 29(2):454-464.
[29] Ku CW, Cheng TS, Ku CO, et al. Distribution and association of interpregnancy weight change with subsequent pregnancy outcomes in Asian women. Sci Rep, 2023, 13(1):4834.
[30] Ziauddeen N, Roderick PJ, Macklon NS, et al. The duration of the interpregnancy interval in multiparous women and maternal weight gain between pregnancies: findings from a UK population-based cohort. Sci Rep, 2019, 9(1):9175.
[31] Thompson ML, Ananth CV, Jaddoe VW, et al. The association of maternal adult weight trajectory with preeclampsia and gestational diabetes mellitus. Paediatr Perinat Epidemiol, 2014,

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

28(4):287-296.

[32] Tano S, Kotani T, Ushida T, et al. Annual Body Mass Index Gain and Risk of Gestational Diabetes Mellitus in a Subsequent Pregnancy. Front Endocrinol (Lausanne), 2022, 13:815390.

[33] Cao J, Xu W, Liu Y, et al. Trends in maternal age and the relationship between advanced age and adverse pregnancy outcomes: a population-based register study in Wuhan, China, 2010-2017. Public Health, 2022, 206:8-14.

[34] Li Y, Ren X, He L, et al. Maternal age and the risk of gestational diabetes mellitus: A systematic review and meta-analysis of over 120 million participants. Diabetes Res Clin Pract, 2020, 162:108044.

[35] Black KI, Schneuer F, Gordon A, et al. Estimating the impact of change in pre-pregnancy body mass index on development of Gestational Diabetes Mellitus: An Australian population-based cohort. Women Birth, 2022, 35(6):563-569.

[36] Teulings NEWD, Masconi KL, Ozanne SE, et al. Effect of interpregnancy weight change on perinatal outcomes: systematic review and meta-analysis. BMC Pregnancy Childbirth, 2019, 19(1):386.

[37] Timmermans YEG, van de Kant KDG, Oosterman EO, et al. The impact of interpregnancy weight change on perinatal outcomes in women and their children: A systematic review and meta-analysis. Obes Rev, 2020, 21(3):e12974.

[38] Kirkegaard H, Bliddal M, Støvring H, et al. Maternal weight change from prepregnancy to 18 months postpartum and subsequent risk of hypertension and cardiovascular disease in Danish women: A cohort study. PLoS Med, 2021, 18(4):e1003486.

For Peer Review Only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

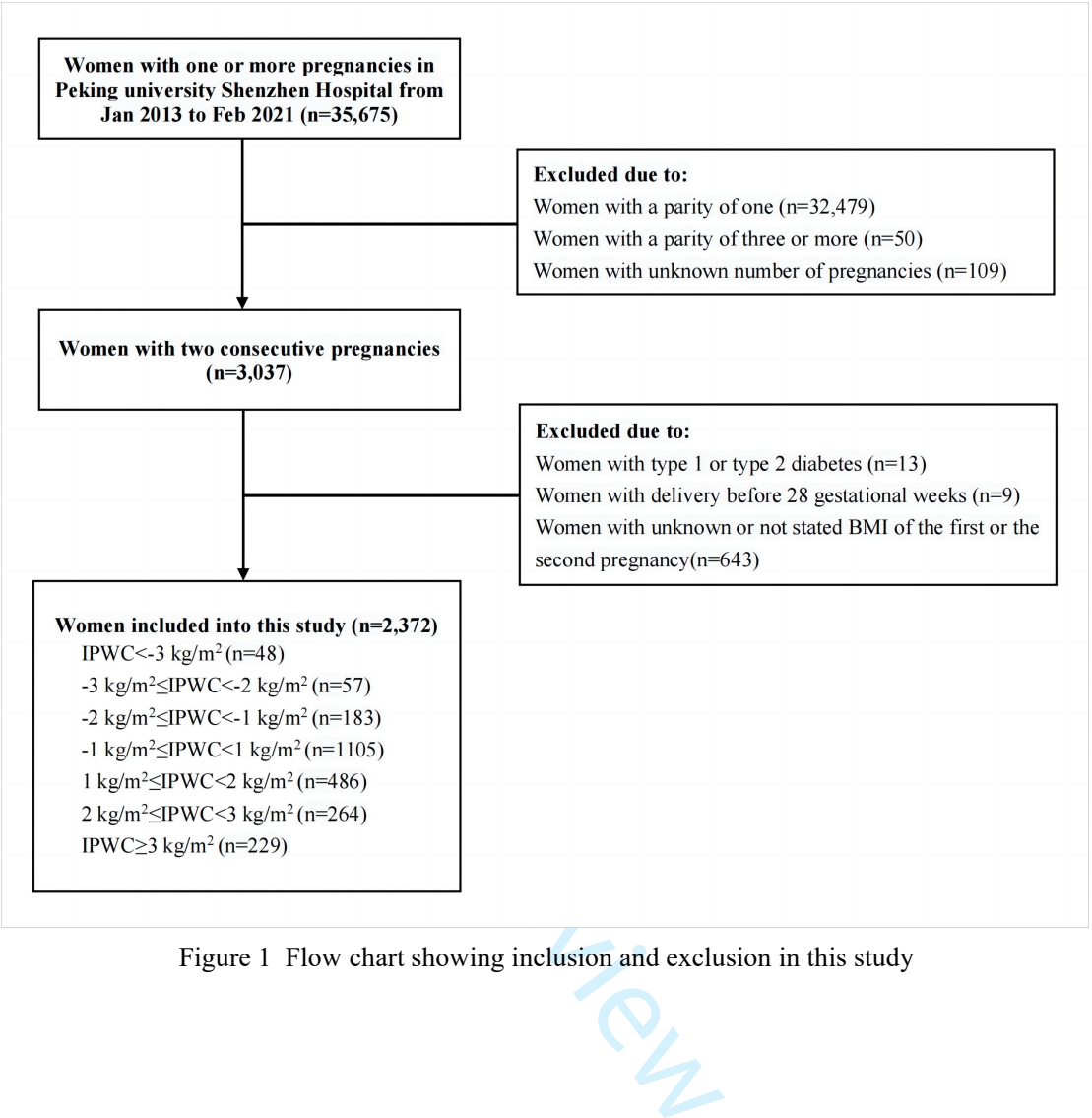


Figure 1 Flow chart showing inclusion and exclusion in this study

View only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

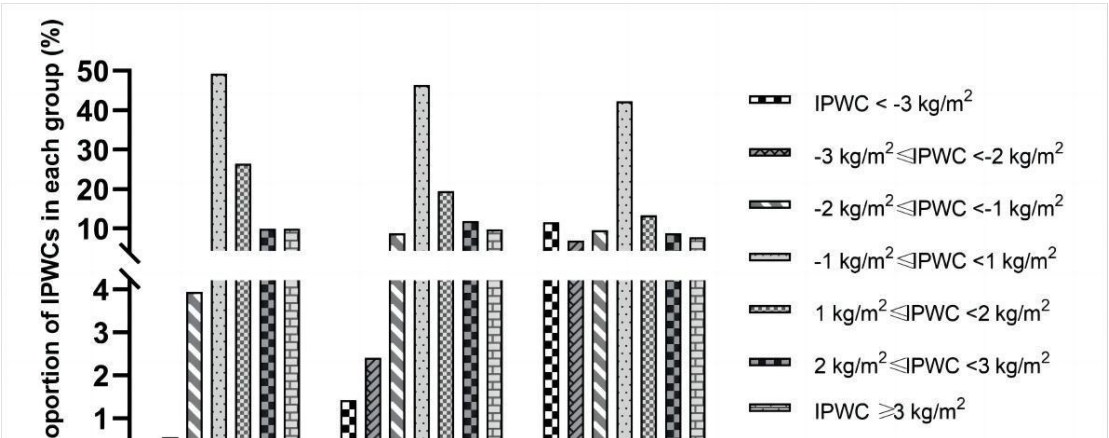


Figure 2 The proportion of individuals in each IPWC category within different groups

Table 1 Univariate analysis of risk factors for the GDM in the second pregnancy

Risk factors	Total (n=2372)	GDM group (n=303)	non-GDM group (n=2069)	$t/Z/\chi^2$	*P*
maternal age (years，x±s)[a]	28.27±3.35	29.29±3.53	28.10±3.28	5.815	0.000
Han nationality	2255(95.07)	289(95.38)	1966(95.02)	0.072	0.788
BMI (kg/m^2)[a]	20.49±2.64	21.33±3.02	20.36±2.55	5.279	0.000
IPWC [kg/m^2 (interquartile range)][b]	0.725(-0.240-1.770)	0.970(-0.150-2.110)	0.680(-0.250-1.730)	2.642	0.008
IPI [months (interquartile range)][b]	31.68(22.50-43.56)	36.16(26.07-48.53)	30.95(22.25-46.25)	4.779	0.000
ART [n (%)][a]	120(5.06)	20(6.6)	100(4.8)	1.719	0.190
GDM [n (%)][a]	265(11.17)	126(41.6)	139(6.7)	323.750	0.000
HDCP [n (%)][a]	81(3.41)	20(6.6)	61(2.9)	2.847	0.092
hypothyroidism [n (%)][a]	132(5.56)	14(4.6)	118(5.7)	0.590	0.443
hyperthyroidism [n (%)][a]	18(0.76)	2(0.7)	16(0.8)	0.045	0.832
APS [n (%)][a]	4(0.17)	0(0)	4(0.2)	0.587	0.444
SLE [n (%)][a]	12(0.51)	0(0)	12(0.6)	1.766	0.184
PPH [n (%)][a]	42(1.77)	8(2.6)	34(1.6)	1.510	0.219
PCOS [n (%)][a]	6(0.25)	2(0.7)	4(0.2)	2.282	0.131
CS [n (%)][a]	735(30.99)	125(41.3)	610(29.5)	17.125	0.000
PTB [n (%)][a]	131(5.52)	23(7.6)	108(5.2)	2.847	0.092
macrosomia [n (%)][a]	99(4.17)	18(5.9)	81(3.9)	2.712	0.100
male newborn [n (%)][a]	1181(49.79)	148(48.8)	1033(49.9)	0.124	0.725

[a] in the first pregnancy; [b] tested by Mann-Whitney *U*-test; BMI: body mass index; IPWC: interpregnancy weight change; IPI: interpregnancy interval; ART: assisted reproductive technology; GDM: gestational diabetes mellitus; HDCP: hypertensive disorder complicating pregnancy; APS: antiphospholipid syndrome; SLE: systemic lupus erythematosus; PPH: postpartum hemorrhage; PCOS: polycystic ovary syndrome; CS:cesarean section; PTB: preterm birth.

For peer review only

Enseignement Superieur (ABES) .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 2 Multivariate analysis of the risk factors for GDM in the second pregnancy

variables	regression coefficient	standard error	Wald value	*P*	*OR*	*95%CI* for *OR*
IPWC < -3 kg/m^2	0.113	0.463	0.059	0.808	1.119	0.452-2.771
-3 kg/m^2≤IPWC <-2 kg/m^2	-0.056	0.453	0.015	0.902	0.946	0.389-2.299
-2 kg/m^2≤IPWC <-1 kg/m^2	-0.124	0.290	0.183	0.669	0.883	0.500-1.560
-1 kg/m^2≤IPWC <1 kg/m^2	reference	reference	reference	reference	reference	reference
1 kg/m^2≤IPWC <2 kg/m^2	0.309	0.175	3.111	0.078	1.363	0.966-1.922
2 kg/m^2≤IPWC <3 kg/m^2	0.212	0.224	0.892	0.345	1.236	0.796-1.918
IPWC ≥3 kg/m^2	0.564	0.217	6.774	0.009	1.758	1.149-2.688
IPI (months)	0.021	0.004	22.632	0.000	1.021	1.012-1.029
Maternal age (years)[a]	0.068	0.021	10.551	0.001	1.070	1.027-1.114
GDM[a]	2.243	0.153	215.010	0.000	9.423	6.982-12.718
HDCP[a]	0.539	0.310	3.028	0.082	1.714	0.934-3.143
macrosomia[a]	0.237	0.300	0.625	0.429	1.267	0.705-2.279
PTB[a]	0.383	0.269	2.024	0.155	1.466	0.865-2.485
CS[a]	0.180	0.146	1.533	0.216	1.198	0.900-1.594

[a] in the first pregnancy; IPI: interpregnancy interval; BMI: body mass index; GDM: gestational diabetes mellitus; HDCP: hypertensive disorder complicating pregnancy; PTB: preterm birth; CS: cesarean section.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

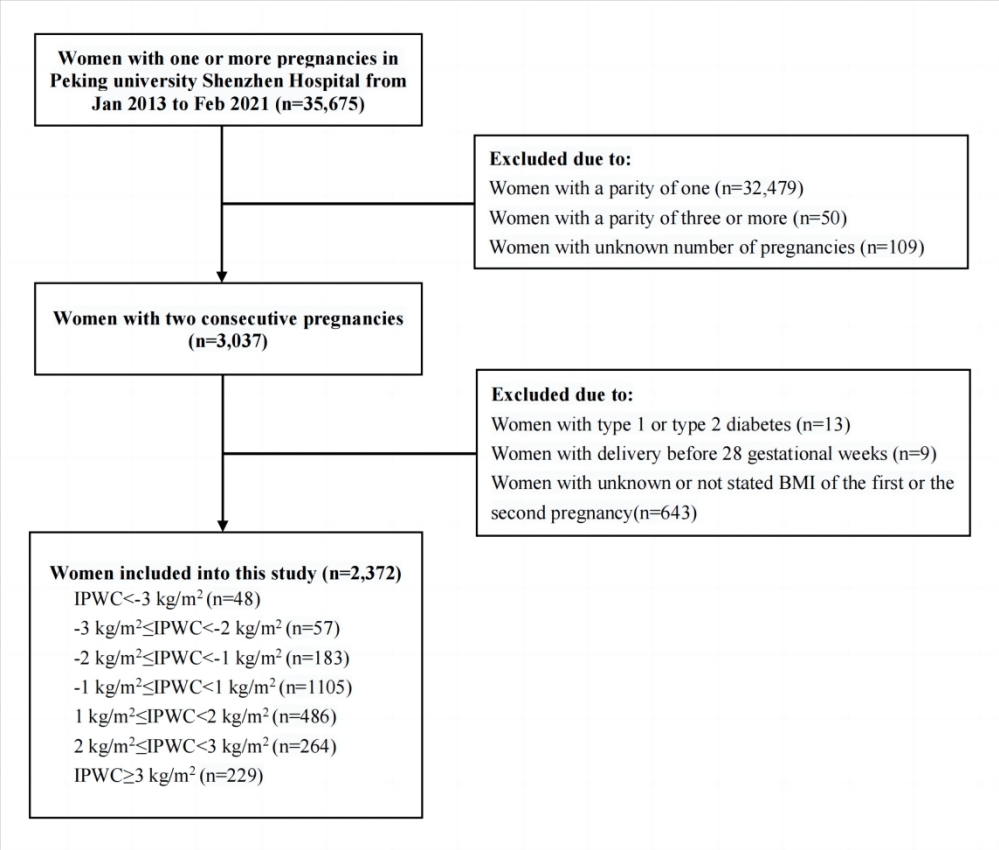
	Adjusted OR and 95%CI						
	IPWC < -3 kg/m²	-3 kg/m²≤IPWC <-2 kg/m²	-2 kg/m²≤IPWC <-1 kg/m²	-1 kg/m²≤IPWC <1 kg/m²	1 kg/m²≤IPWC <2 kg/m²	2 kg/m²≤IPWC <3 kg/m²	IPWC ≥3 kg/m²
IPI≤36 months (n=1426)	0.817(0.192-3.47)	0.763(0.21-2.772)	1.045(0.499-2.189)	1.000	1.419(0.865-2.328)	0.893(0.444-1.799)	**2.165(1.214-3.860)**
IPI>36 months (n=946)	1.504(0.454-4.984)	1.272(0.362-4.465)	0.741(0.305-1.799)	1.000	1.342(0.828-2.175)	1.612(0.900-2.888)	1.441(0.767-2.705)
BMI ≤21 kg/m² (n=1534)[a]	-	-	0.909(0.367-2.251)	1.000	1.52(0.985-2.345)	1.192(0.659-2.156)	1.591(0.915-2.769)
BMI >21 kg/m² (n=838)	0.961(0.382-2.417)	0.892(0.349-2.278)	0.794(0.381-1.658)	1.000	1.161(0.650-2.072)	1.281(0.659-2.490)	**2.256(1.135-4.483)**
maternal age≤30 years(n=1810)	0.665(0.176-2.513)	0.816(0.255-2.616)	0.628(0.295-1.336)	1.000	1.307(0.868-1.968)	1.473(0.907-2.391)	1.609(0.973-2.660)
maternal age>30 years (n=562)	2.275(0.56-9.246)	1.059(0.254-4.423)	1.672(0.668-4.183)	1.000	1.593(0.831-3.054)	0.555(0.188-1.634)	**2.381(1.054-5.377)**

Table 3 Adjusted OR values of IPWC for the GDM risk in the second pregnancy in stratified analysis

[a] In this subgroup, there were no cases of GDM in the second pregnancy if the IPWC was less than -2 kg/m².

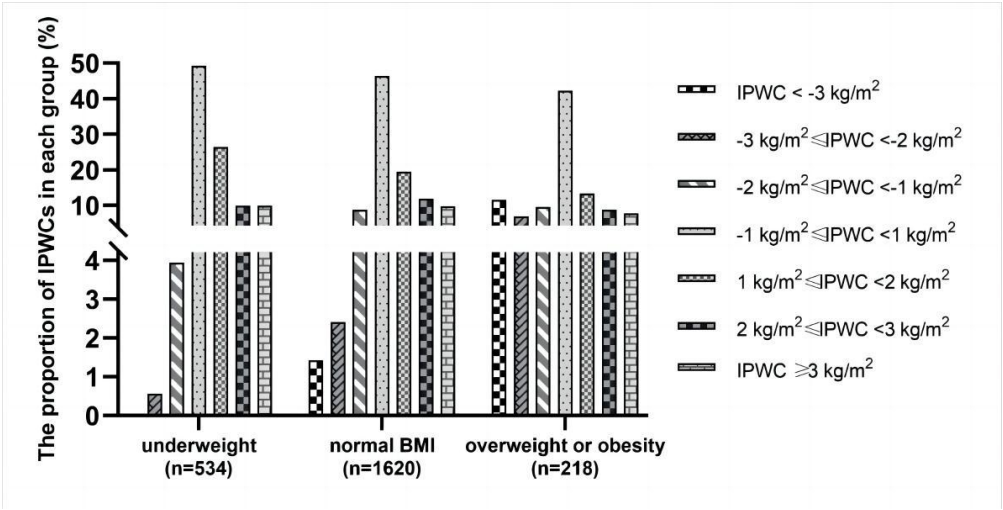
For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .



519x442mm (144 x 144 DPI)

BMJ Open: first published as 10.1136/bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.



209x106mm (144 x 144 DPI)

BMJ Open: first published as 10.1136/bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open

The impact of interpregnancy weight change on the risk of gestational diabetes mellitus during a second pregnancy in Chinese population：a retrospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-084282.R1
Article Type:	Original research
Date Submitted by the Author:	06-Nov-2024
Complete List of Authors:	Yang, Ao; Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital; Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center; Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases Wang, Ying; Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital; Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center; Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases Liu, Yuzhen; Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Center of Obstetrics and Gynecology; Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center; Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases Yang, Juan; Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital; Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center; Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases Xu, Chang; Intelligent Hospital Research Academy, Peking University Shenzhen Hospital Zhong, Shilin; Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital; Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center; Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases
Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Obstetrics and gynaecology
Keywords:	Diabetes in pregnancy < DIABETES & ENDOCRINOLOGY, OBSTETRICS, Weight Gain, Maternal medicine < OBSTETRICS, Risk Factors

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

The impact of interpregnancy weight change on the risk of gestational diabetes mellitus during a second pregnancy in Chinese population：a retrospective cohort study

Ao Yang[1,2,3 *], Ying Wang[1,2,3 *], Yuzhen Liu[1,2,3 *], Juan Yang[1,2,3], Chang Xu[4], Shilin Zhong[1,2,3]

[1]Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China.
[2]Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen, Guangdong, China.
[3]Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases, Shenzhen, Guangdong, China.
[4]Intelligent Hospital Research Academy, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China.
[*]Ao Yang, Ying Wang and Yuzhen Liu contributed equally to this article.

Correspondence
Shilin Zhong, Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, 1120 Lianhua Road, Shenzhen 518036, Guangdong, China.
Email: zhongshilin2013@163.com

Abstract

Objectives This study aimed to investigate the impact of interpregnancy weight changes (IPWC) on the risk of gestational diabetes mellitus (GDM) in the second pregnancy.

Design A retrospective cohort study.

Setting Data were collected in Peking University Shenzhen Hospital from 2013 Jan to 2021 Feb.

Participants Women who had two consecutive singleton deliveries after 28 gestational weeks (N=2372).

Outcomes The risk of GDM in the second pregnancy.

Methods: IPWC was divided into seven categories by units BMI (kg/m^2), with the range of -1 kg/m^2 to 1 kg/m^2 being used as the reference range. Adjusted odds ratios (aORs) with 95% CIs were obtained by multivariable logistic regression models to evaluate the association between the IPWC and GDM. Analyses were stratified by interpregnancy interval (IPI), maternal age, GDM, BMI in the first pregnancy.

Results: IPWC is significantly positively associated with the GDM during the second pregnancy (aOR 1.443 [95% CI 1.026-2.031] for BMI gain of 1 to 2 kg/m^2; aOR 1.818 [95% CI 1.194-2.767] for BMI gain of ⩾3 kg/m^2; aOR 1.111 [95% CI 1.038-1.190] for per unite increase of continuous IPWC). No significant link was found between interpregnancy BMI decrease and GDM risk (P>0.05). Stratified analysis revealed that the significant association between IPWC ⩾3 units and GDM risk was only showed in participants with IPI less than 36 months (aOR 2.217, 95%CI 1.254-3.922), maternal age under 35 years (aOR 1.850, 95%CI 1.201-2.849), those without GDM

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

(aOR 1.867, 95%CI 1.140-3.056) and those with normal weight (aOR 1.933, 95%CI 1.171-3.190) in the first pregnancy. The continuous IPWC was significantly associated with GDM only within these same subgroups (P<0.05). A decline in IPWC showed no significant relationship with GDM risk across any subgroups (P>0.05).

Conclusion: An increase of 3 or more units in IPWC may pose a risk for GDM in the second pregnancy, particularly among younger women with shorter IPI, who had normal weight and no GDM during their first pregnancy.

Keywords gestational diabetes mellitus, interpregnancy weight change, risk factor, maternal age, interpregnancy interval

Strength and limitations of this study

► The association between both categorical and continuous IPWC values and GDM during a second pregnancy was examined in a cohort of 2,372 cases involving consecutive singleton births in China.

► Two models were used to control for confounders, and they did not alter the primary results.

► Stratified analysis was performed based on IPI, maternal age, GDM, and BMI during the first pregnancy, and the interaction effects between IPWC and these stratified factors were examined.

► The main limitation is the retrospective design, and the data of diet, family history of diabetes, and gestational weight gain during the first pregnancy, were not included in the analysis.

► The sample size for certain subgroups is relatively small.

INTRODUCTION

Gestational diabetes (GDM) is a type of diabetes that develops during pregnancy. In China, the prevalence of GDM is as high as 14.8%[1],leading to adverse consequences for both the mother and the fetus. Consequently, it is crucial to implement preventive actions to effectively manage the occurrence of diabetes in advance, yielding significant clinical relevance.

The occurrence of GDM is influenced by various factors, such as weight[2], diet[3], maternal age[4], exercise, and genetics[5]. Weight is particularly significant in relation to GDM development. Excessive weight gain during pregnancy proves to be a major risk factor for GDM[6,7]. Research conducted in China highlights the close relationship between pregestational weight and GDM[8].

Several studies indicate a significant correlation between interpregnancy weight changes (IPWC) and gestational diabetes mellitus (GDM) [9, 10, 11, 12, 13]. However, there is no consensus on the precise impact of BMI changes on GDM risk. In 2019-2021, systematic analyses by Teulings et al. [14], Timmermans et al. [15], and Nagpal et al. [16] confirmed the positive association between IPWC and GDM risk. Nevertheless, these studies did not find that weight loss between pregnancies reduced GDM risk. Conversely, Oteng-Ntim et al.'s systematic review[17] suggested the protective effect of reducing IPWC on GDM. Timmermans et al. [15] identified that an IPWC of 1 to 3 units correlates with an odds ratio (OR) of 1.64 [95% CI 1.28-2.11] for GDM in the second pregnancy, and IPWC of ⩾3 units with an OR of 2.42 [95% CI 1.62-3.62]. However, three out of five studies gathered data prior to 2010, and the remaining two included some pre-2010 cases. Given that current GDM diagnostic criteria in China were recommended by the IADPSG in 2010[18], these studies' applicability to the Chinese population warrants reevaluation. Furthermore, most existing studies lack stratified analyses based on interpregnancy interval (IPI) or maternal

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

age. Variations in study populations could lead to differing results, and there is a notable absence of large-scale studies within the Chinese demographic. Consequently, further investigation among the Chinese population is essential.

Since 2016, China's two-child policy has been implemented to stimulate a rise in fertility levels. It has been found that 37% of couples have expressed intentions to have a second child[19]. A higher proportion of advanced maternal age (>30 years) and multiparity have increased the risk of GDM[20]. The interpregnancy period is a critical time of health improvement and weight control to reduce the risk of GDM in a second pregnancy [21,22]. Regardless of whether they have had diabetes in their first pregnancy, both women and their physicians are interested in determining the ideal weight control target to minimize the risk of GDM in future pregnancies.

Therefore, we conducted a single-center, retrospective study in China to analyze the impact of weight change during two pregnancies on the risk of GDM in the second pregnancy. Our study indicates that a BMI increase of 3 units or more may be significantly linked to the risk of GDM in the Chinese population. These findings may offer guidance for weight management objectives.

MATERIALS ADN METHODS

Study design and Population

We conducted a retrospective cohort study on participants who had two consecutive single deliveries after 28 weeks at Peking University Shenzhen Hospital from 2013, Jan to 2021, Feb. Exclusion criteria for this study included women who had multiple pregnancies, women with a parity of one, women with a parity of three or more, women who delivered before 28 gestational weeks, women without available BMI data, women with type 1 or type 2 diabetes, and women with unknown or unstated BMI for their first or second pregnancy. The study protocol was approved by the Medical Ethics Committee of Peking University Shenzhen Hospital (#2023-103). The participants were classified into two groups based on whether their second pregnancy was complicated by GDM: the GDM group and the non-GDM group.

Patient and Public Involvement statement

None

Definitions of the Variable and outcome

In this study involving two pregnancies, we designated the earlier pregnancy as "the first pregnancy" and the latter as "the second pregnancy." The primary variable examined was interpregnancy weight change (IPWC), defined as the difference in body mass index (BMI) between the first trimester of the second pregnancy and that of the first pregnancy[23]. IPWC, expressed in BMI units (kg/m^2), was categorized into seven groups: $\leqslant$-3 kg/m^2, -3 kg/m^2 to <-2 kg/m^2, -2 kg/m^2 to <-1 kg/m^2, -1 kg/m^2 to <1 kg/m^2 (considered stable BMI and used as a reference), 1 kg/m^2 to <2 kg/m^2, 2 kg/m^2 to < 3 kg/m^2, and $\geqslant$3 kg/m^2. Participants were classified into four BMI categories: underweight (<18.5 kg/m^2), normal weight (18.5 kg/m^2 to <24.0 kg/m^2), and overweight or obese ($\geqslant$24.0 kg/m^2). The interpregnancy interval was defined as the duration in months between the end of one pregnancy and the start of the next, calculated by subtracting the gestational age at the second delivery from the interval between the delivery dates

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

of two consecutive pregnancies [23]. Advanced maternal age was described as being 35 years or older [24].

The primary outcome of the study was the presence of GDM in the second pregnancy. Throughout the entire study period, GDM was diagnosed using the IADPSG criteria[25], which involved a 75-gram oral glucose tolerance test. According to these criteria, a diagnosis of GDM was made if the serum blood glucose levels were ⩾5.1 mmol/L at 0 hour, and/or ⩾10.0 mmol/L at 1 hour, and/or ⩾8.5 mmol/L at 2 hour, between 24-28 weeks of gestation.

Data collection

The data for this study were obtained from the delivery records within the hospital information system. The collected variables include: IPI, maternal age, BMI, parity, year of delivery, delivery mode, occupation, medical payment method, ethnicity, marital status, sex of newborn, birth weight, BMI of the first trimester during the first and second pregnancies, and the occurrence of GDM, thyroid disease, hypertensive disorder complicating pregnancy (HDCP), and preterm birth.

Methods of analysis

Initially, we analyzed the magnitude or proportion of continuous IPWC and IPWC categories and other factors in the GDM and non-GDM subjects. These factors included the continuous IPWC value, IPWC categories, BMI during the first trimester, interpregnancy interval (IPI), maternal age, nationality, gender of the newborn, presence of GDM, hypertensive disorder complicating pregnancy (HDCP), use of artificial reproduction technology, incidence of polycystic ovary syndrome, macrosomia, preterm delivery, cesarean section at first pregnancy, and the BMI during the first trimester of the second pregnancy. Subsequently, we applied both univariable and multivariable logistic regression models to assess the impact of IPWC on GDM risk in the second pregnancy, reporting both unadjusted and adjusted odds ratios with 95% confidence intervals. Two multivariable regression models were employed to control for confounding factors. Confounders with a significant difference ($P < 0.1$) from the univariable analysis underwent collinearity assessment, with those having a variance inflation factor (VIF) < 10 deemed to have low collinearity and thus included in model 1 of the logistic multivariable regression. We then individually evaluated the impact of each confounder from model 1 on the effect of IPWC. Confounders altering the odds ratio (OR) of IPWC on GDM by more than 10% were incorporated into model 2 of the logistic multivariable regression.

Stratified analysis was performed to evaluate the impact of IPWC on GDM risk within specific subgroups categorized by IPI, maternal age, GDM status, and BMI during the first pregnancy. The population was divided based on IPI (IPI < 36 months, IPI ⩾ 36 months) [26], maternal age (⩾ 35 years, < 35 years), GDM status in the first pregnancy (GDM, non-GDM), and BMI in the first trimester of the first pregnancy (overweight or obese, normal weight, underweight). Additionally, this study separately analyzed the interaction between continuous and categorical IPWC with these four stratification factors.

Statistical method

The data analysis was performed using SPSS 24.0 statistical software (IBM, Armonk, NY, USA). Categorical variables were presented as n (%) and compared using the Chi-square test.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Normally distributed variables were presented as mean ± standard deviation and compared using the student's *t*-test. Non-normally distributed variables were presented as median (interquartile range; IQR) and compared using the Mann-Whitney *U* test. Multivariable logistic regression models were used to assess the association between the independent variable (IPWC) and the risk of GDM in the second pregnancy, adjusting for selected confounders in model 1 and model 2, respectively. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

Baseline characteristics of the subjects

A total of 35,675 participants who had experienced at least one pregnancy at Peking University Shenzhen Hospital were recorded between January 2013 and February 2021. After disqualifying 33,303 participants based on the exclusion criteria, a final cohort of 2,372 participants who had undergone two consecutive single deliveries were included (Figure 1).

During the first pregnancy, the average age of participants was 28.25 ± 3.33 years, with a mean BMI of 20.48 ± 2.64 kg/m² and an average gestational age at delivery of 38.82 ± 1.53 weeks. Among them, 534 individuals (22.51%) were underweight, 1,620 (68.30%) had normal weight, and 218 (9.19%) were categorized as overweight or obese. There were 265 instances (11.17%) of GDM. The incidence of GDM in advanced-age pregnancies (23 of 86, 26.74%) was significantly higher than that in younger pregnancies (242 of 2,286, 10.59%) ($\chi^2 = 21.805$, $P < 0.001$). Similarly, the rate of GDM was significantly higher among overweight or obese women (54 of 218, 24.77%) compared to women of normal weight (165 of 1,620, 10.19%) ($\chi^2 = 38.946$, $P < 0.001$).

In the second pregnancy, the average age was 31.15 ± 3.57 years, with a mean BMI of 21.27 ± 2.90 kg/m² and a mean gestational age at delivery of 38.54 ± 1.45 weeks. Of these, 371 cases (15.64%) were categorized as underweight, 1,620 (68.30%) had normal weight, and 381 (16.06%) were overweight or obese. A total of 303 cases (12.77%) were diagnosed with GDM.

The interpregnancy weight change (IPWC) of the subjects

The median IPWC was 0.725 kg/m² (P25: -0.240 kg/m² ; P75: 1.770 kg/m²). There were 48, 57, 183, 1105, 183, 486, 264, and 229 cases with IPWC values of ≤ -3 kg/m² , ranging from -3 kg/m² to <-2 kg/m² , from -2 kg/m² to <-1 kg/m² , from -1 kg/m² to <1 kg/m² , from 1 kg/m² to <2 kg/m² , from 2 kg/m² to <3 kg/m² , and > 3 kg/m² , respectively. Among underweight women in the first trimester, approximately 50% maintained a stable IPWC, 4.49% had an IPWC of ≤ -1 kg/m² , and 46.25% had an IPWC greater than 1 kg/m² . About 42% of women who were overweight or obese in the first trimester maintained a stable IPWC, while 27.98% had an IPWC of ≤ -1 kg/m² and 29.82% had an IPWC greater than 1 kg/m² . Interestingly, the proportion of those with an IPWC > 2 kg/m² did not significantly differ between overweight/obese and underweight women (Table 1). Furthermore, the variation in IPWC was not significantly affected by the presence of GDM during the first pregnancy (Table 1).

Univariable analysis of the risk factors for the GDM in the second pregnancy

In the GDM group, maternal age, BMI, continuous IPWC value, and IPI (in months) were all significantly higher than in the non-GDM group ($P < 0.01$, Table 2). Furthermore, the GDM group had a higher proportion of GDM cases and CS deliveries compared to the non-GDM group ($P < 0.01$, Table 2). Among underweight, normal weight, and overweight or obese participants, 8.61% (46/534), 10.19% (165/1620), and 24.77% (54/218), respectively, were affected by GDM. In the

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

second pregnancy, the prevalence of GDM was 7.55% (28/371), 11.98% (194/1620), and 21.26% (81/381) for the same categories, respectively. The proportion of stable IPWC in the GDM group was significantly lower than in the non-GDM group ($\chi2$=4.474, P=0.034), while the proportion of IPWC ⩾3 units was significantly higher ($\chi2$=7.049, P=0.008) (Table 1). There were no significant differences in the proportions of other IPWC categories between the GDM and non-GDM groups (Table 1).

The effect of the IPWC categories and continuous IPWC value on the GDM in the second pregnancy

BMI in the first trimester, continuous interpregnancy interval (IPI), maternal age, gestational diabetes mellitus (GDM), hypertensive disorders in pregnancy (HDCP), macrosomia, preterm delivery, and cesarean delivery in the first pregnancy were included in Model 1 after univariable and collinearity analyses (Table S1). Subsequently, the BMI in the first trimester and GDM in the first pregnancy were included in Model 2 to assess the impact of confounding factors on the OR value of IPWC concerning GDM (Table S2). In both unadjusted and adjusted models (Model 1 and Model 2), IPWC ⩾3 kg/m² was independently linked to an elevated risk of GDM in the second pregnancy compared to the reference IPWC (Table 3). Additionally, the adjusted models indicated that an IPWC between 1 kg/m² and <2 kg/m² was also associated with a higher risk of GDM in the second pregnancy, whereas other IPWC categories showed no significant correlation with GDM (Table 3). Without adjusting for any confounders, the OR for continuous IPWC value concerning GDM in the second pregnancy was 1.067 (95% CI: 1.000-1.139) (P=0.05). After adjusting for confounders (whether in Model 1 or Model 2), continuous IPWC value was significantly associated with GDM in the second pregnancy (Table 4).

The stratified analysis for the effect of the IPWC on the GDM in the second pregnancy

IPWC ⩾3 kg/m² was strongly linked to a heightened risk of GDM in second pregnancies for individuals with an IPI of less than 36 months, maternal age under 35, absence of GDM, and normal first-trimester weight during their first pregnancy, regardless of model 1 or model 2 (Table 5). Furthermore, model 1 demonstrated that an IPWC between 1 kg/m² and <2 kg/m² was significantly associated with GDM risk in women without GDM in their first pregnancy. Meanwhile, model 2 indicated this IPWC range was significantly associated with GDM risk not only in non-GDM women but also in those with a maternal age under 35 during their first pregnancy (Table 5). Conversely, no association was found between any IPWC categories and GDM risk in participants with IPI ⩾ 36 months, maternal age ⩾35, existing GDM, or those who were overweight, obese, or underweight during their first pregnancy. Additionally, no significant link was detected between an IPWC of less than -1 kg/m² and GDM risk across any subgroups, aligning with the overall study findings (Table 5).

Continuous IPWC values were significantly linked to an increased risk of GDM in the second pregnancy, similar to the findings for IPWC values of ⩾3 kg/m² (Table 4). However, in subgroups such as those with an IPI ⩾36 months, advanced maternal age, previous GDM, or first pregnancy weight classification as overweight, obese, or underweight, no significant association was observed between any IPWC category or continuous IPWC value and GDM risk in the second pregnancy. To enhance the sample size, we consolidated all categories with an IPWC of less than -1 kg/m² into a single category. Nonetheless, this category did not demonstrate a

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

significant association with GDM risk in any subgroup, whether considered overall or within stratified analyses (Table S3). Additionally, neither the IPWC categories (Table S4) nor continuous IPWC values (Table S5) showed significant interactions with the four stratification factors.

DISCUSSION

This single-center study in China highlights a strong link between the risk of GDM in second pregnancies and an increase in BMI of at least 3 units. Stratified analysis confirmed this association for participants with an IPI of 36 months or less, maternal age under 35, no previous GDM, and normal weight in their first pregnancy. This study provides valuable guidance for women aiming to prevent GDM in their second pregnancy by setting weight management goals. Conversely, we did not observe this association in those with an IPI of 36 months or more, maternal age of 30 or older, a history of GDM, or those who were overweight, obese, or underweight during their first pregnancy. Additionally, no correlation was found between GDM risk and a decrease in BMI.

The study identified a significant positive effect of IPWC $\geqslant$ 3 kg/m^2 on GDM in the second pregnancy across two different models, underscoring the reliability of this finding. However, for the category 1 kg/m^2 $\leqslant$ IPWC<2 kg/m^2, despite an overall significant association with GDM, stratified analysis indicated this result was confirmed only in younger patients (<35 years) or those without GDM in their first pregnancy. Consequently, the association between 1 kg/m^2 $\leqslant$ IPWC<2 kg/m^2 and GDM remains uncertain, and further research is needed to determine whether this effect is influenced by other factors.

Being overweight or obese prior to pregnancy is a significant risk factor for GDM[8]. Insulin resistance plays a crucial role in the development of GDM among individuals who are overweight[27]. Furthermore, excessive gestational weight gain (GWG) is closely linked to the occurrence of GDM[7,8].To mitigate the risk of GDM and macrosomia, the Institute of Medicine (IOM) suggests adopting appropriate GWG guidelines for single pregnancies based on pre-pregnancy weights[28]. Moreover, substantial weight gain before pregnancy has also been found to be associated with GDM[29].

Over the past decade, several studies conducted in different countries have suggested a potential link between interpregnancy weight change (IPWC) and the risk of GDM[17,16]. Whiteman et al.'s study identified a significant association between changes in BMI classification, particularly from normal to overweight or obese, and the risk of GDM[30]. Participants who experienced an increase in BMI had higher odds of developing GDM compared to those whose BMI remained unchanged[31]. In addition, the magnitude of the change in BMI was also thought to be associated with GDM risk. Earlier investigations suggested that an increase of 3 or more units in BMI substantially increased the likelihood of developing GDM, when compared to the stable IPWC categories (±1kg/m^2) [11]. Subsequent research by Bogaerts et al[9]. and Knight-Agarwal et al[32]. also confirmed this finding, which is consistent with the results in our study.

Additional observational studies[12,13, 33, 34] and two systematic reviews[16,35] have suggested that even a single-unit increase in BMI is linked to a higher risk of GDM. The smaller IPWC values found to significantly correlate with GDM risk in these studies, compared to the present study, could be due to variations in population criteria[34], diverse diagnostic standards for GDM[12,13, 33, 34], differing definitions of IPWC[33], or distinct confounding factors considered in relation to GDM[33, 13, 34]. It is essential to note

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

that the outcomes of these studies may differ among various study groups. Our study, conducted within the Chinese population, enhances the findings of previous research largely centered on populations in developed countries. Furthermore, our results indicate that the risk of GDM in subsequent pregnancies increases by approximately 11% for each unit increase in IPWC as a continuous variable, aligning with findings by Lyne Lynes et al. (OR=1.08, 95%CI: 1.05-1.10) [12]. Therefore, we suggest that controlling IPWC, especially IPWC more than 3 units, may be effective in reducing the risk of GDM in the next pregnancy in Chinese population.

Unlike the overall study results, the results of stratified analysis suggests that the impact of IPWC on GDM varies in different subgroups. Even with a similar increase in BMI of three units or more, the risk of GDM differs based on IPI, maternal age, GDM status, or BMI in the first pregnancy. Stratified analysis revealed that an increase in BMI of three units or more had a more significant impact on the risk of GDM in participants with a shorter IPI compared to those with a longer IPI. Compared to an interval of 24 to 35 months, an interval ⩾36 months was associated with a higher risk of weight gain from the first to the second pregnancy[36]. Previous studies have also shown that women with GDM tend to gain weight faster before pregnancy compared to non-GDM women[37]. Therefore, it would be more reasonable to investigate the association between weight change and GDM within a narrower range of IPI[9]. Tano et al. 's study suggested that annual BMI gain was associated with the risk of GDM during the subsequent pregnancy[38]. These studies imply that the risk of GDM is not only associated with increased BMI units but also with the rate at which BMI increases by three units or more. The effect of IPI on GDM risk diminishes after 36 months between pregnancies.

In the stratified analysis by maternal age, our study identified a significant association between an IPWC of ⩾ 3 units and an increased risk of GDM in women under 35, but not in older women. For those with advanced maternal age, the incidence of GDM in their first pregnancy significantly rose, with GDM in a previous pregnancy being the most significant risk factor for GDM in the second pregnancy (OR:9.884), potentially masking the effect of IPWC. A study conducted in China found that women over the age of 30 had a higher risk of GDM compared to women aged 25 to 29 years old [39]. Additionally, the risk of GDM in Asian women was more strongly correlated with age starting at 25 years old, compared to Europid women[40]. Regrettably, no other stratified studies based on maternal age were identified in the existing literature. This finding has important implications in establishing weight control goals based on age. To further validate this hypothesis, further research with a larger sample size is necessary.

Similarly, stratified analysis based on BMI during the first pregnancy revealed that the association between IPWC and GDM was significant only in normal-weight women, with no significant link found in those who were overweight or obese. This contrasts with the findings of McBain et al. [6] and Ku et al. [34], who reported a significant relationship between IPWC and GDM across all BMI subgroups, with the larger IPWC category showing increased GDM risk particularly in the lower BMI subgroup. However, McBain et al. [6] used the interval -2 kg/m^2 < IPWC < 2 kg/m^2 as a reference and defined overweight or obesity as BMI⩾25 kg/m^2, while Ku et al. [34] used a BMI cutoff of 23 kg/m^2, potentially contributing to the differences in outcomes. Given that overweight or obese women in our study had a higher GDM risk during the first pregnancy ($P < 0.001$), we hypothesized that the absence of a significant IPWC-GDM association in the second pregnancy among these women might stem from the influence of GDM during the first pregnancy. Although we did not find an interaction between IPWC and BMI categories, the

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

possibility of an interaction involving IPWC, BMI category, and GDM status in the first pregnancy remains open for larger sample investigation. One study that stratified analyses by BMI and GDM status in the first pregnancy found that for overweight or obese women with GDM in their first pregnancy, the risk of GDM in a subsequent pregnancy was markedly higher if IPWC was ⩾4 units [41]. Conversely, without GDM in their first pregnancy, an IPWC >1 unit heightened their GDM risk in the second pregnancy[41]. Collectively, these findings imply that IPWC has a more pronounced impact on GDM risk in normal-weight women compared to those overweight or obese. The lack of an effect of IPWC on GDM in women who were underweight during their first pregnancy may be attributed to the necessity for greater weight gain to achieve a normal weight [42], thus not elevating GDM risk.

Our study did not find evidence to support the protective effect of weight loss on GDM, which is consistent with the findings of other studies[12, 13, 32, 34]. To address potential negative results due to small sample size, categories with an IPWC of less than −1 kg/m² were combined to increase sample size. Nonetheless, this combined category still did not show an association with GDM in the second pregnancy. We hypothesize that women with decreased IPWC might possess intrinsic risk factors for GDM, possibly related to their efforts in weight control, thereby not significantly reducing GDM risk in subsequent pregnancies. Three systematic analyses also yielded consistent results[14, 15, 17]. However, Martinez-Hortelano et al.'s stratified analyses suggest a decline in initial pre-pregnancy weight significantly reduced the risk of GDM in women with a body mass index (BMI) greater than 25kg/m^2 during their first pregnancy. This effect was not observed in women with a BMI less than 25kg/m^2 [35]. Conversely, a systematic analysis by Kirkegaard et al. found the opposite association: in women with a BMI less than 25 kg/m^2, a decrease in BMI was significantly associated with increased GDM risk[43]. Interestingly, Black et al.'s study found that for underweight or normal weight women with GDM in their first pregnancy, a decrease in BMI significantly increased the risk of GDM in a second pregnancy by 31% compared to maintaining a stable BMI [41]. These studies reveal ongoing uncertainty regarding the association between weight loss and GDM risk in different participant populations.

Certainly, this study has several limitations. Firstly, it is a retrospective, single-center study, with all data collected from historical databases. Some confounding factors, such as diet, family history of diabetes, and gestational weight gain during the first pregnancy, were not included in the analysis, potentially impacting the results. Secondly, the sample size for certain subgroups, such as those who are overweight or obese and those with GDM in their first pregnancy with a BMI increase of three units or more, is relatively small, reducing statistical power. Thirdly, excluding women without BMI information may have introduced selection bias.

CONCLUSION

Our study conducted in China identified a significant association between an increase of 3 or more BMI units between two pregnancies and the risk of GDM during the second pregnancy. This was especially evident in women with an interpregnancy interval of less than 36 months, maternal age under 35 years, no GDM, or normal weight in the first pregnancy. Additionally, we found no link between the risk of GDM and a decrease in IPWC. To achieve more definitive results, further research with a larger sample size is necessary, particularly focusing on groups that are overweight, obese, underweight, as well as the GDM subgroup in the first pregnancy.

For peer review only

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Acknowledgments The authors thank all the participants in this study

Contributors SZ designed the study, supervised the work, reviewed and edited the manuscript. AY, YW, YL and JY collected the clinical data. AY, YW, YL and CX researched the data, performed the statistical analysis and wrote the manuscript. SZ is the guarantor. All authors have read and approved the final manuscript.

Funding This study was granted by the Shenzhen Science and Technology Innovation Program (JCYJ20210324110206017), the research project of Peking University Shenzhen Hospital (LCYJ2021010), Sanming Project of Medicine in Shenzhen (No.SZSM202011016) and Shenzhen High-level Hospital Construction Fund (YBH2019-260).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study protocol was approved by the Medical Ethics Committee of Peking University Shenzhen Hospital (#2023-103).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

References

1. Gao C, Sun X, Lu L, Liu F, Yuan J. Prevalence of gestational diabetes mellitus in mainland China: A systematic review and meta-analysis. *J Diabetes Investig*. 2019;10(1):154-162. doi:10.1111/jdi.12854
2. Goldstein RF, Abell SK, Ranasinha S, et al. Gestational weight gain across continents and ethnicity: systematic review and meta-analysis of maternal and infant outcomes in more than one million women. *BMC Med*. 2018;16(1):153. doi:10.1186/s12916-018-1128-1
3. Yamamoto JM, Kellett JE, Balsells M, et al. Gestational Diabetes Mellitus and Diet: A Systematic Review and Meta-analysis of Randomized Controlled Trials Examining the Impact of Modified Dietary Interventions on Maternal Glucose Control and Neonatal Birth Weight. *Diabetes Care*. 2018;41(7):1346-1361. doi:10.2337/dc18-0102
4. Zhang Y, Xiao CM, Zhang Y, et al. Factors Associated with Gestational Diabetes Mellitus: A Meta-Analysis. *J Diabetes Res*. 2021;2021. doi:10.1155/2021/6692695
5. Wu L, Cui L, Tam WH, Ma RCW, Wang CC. Genetic variants associated with gestational diabetes mellitus: a meta-analysis and subgroup analysis. *Sci Rep*. 2016;6:30539. doi:10.1038/srep30539
6. McBain RD, Dekker GA, Clifton VL, Mol BW, Grzeskowiak LE. Impact of inter-pregnancy BMI change on perinatal outcomes: a retrospective cohort study. *Eur J Obstet Gynecol Reprod Biol*. 2016;205:98-104. doi:10.1016/j.ejogrb.2016.07.487
7. Peng Y, Han N, Su T, et al. Gestational weight gain and the risk of gestational diabetes mellitus: A latent class trajectory analysis using birth cohort data. *Diabetes Res Clin Pract*. 2021;182:109130. doi:10.1016/j.diabres.2021.109130
8. Sun Y, Shen Z, Zhan Y, et al. Effects of pre-pregnancy body mass index and gestational weight

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

gain on maternal and infant complications. *BMC Pregnancy Childbirth*. 2020;20(1):390. doi:10.1186/s12884-020-03071-y

9. Bogaerts A, Van Den Bergh BRH, Ameye L, et al. Interpregnancy weight change and risk for adverse perinatal outcome. In: *Obstetrics and Gynecology*. Vol 122. ; 2013:999-1009. doi:10.1097/AOG.0b013e3182a7f63e
10. Ehrlich SF, Hedderson MM, Feng J, Davenport ER, Gunderson EP, Ferrara A. Change in body mass index between pregnancies and the risk of gestational diabetes in a second pregnancy. *Obstet Gynecol*. 2011;117(6):1323-1330. doi:10.1097/AOG.0b013e31821aa358
11. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. *Lancet (London, England)*. 2006;368(9542):1164-1170. doi:10.1016/S0140-6736(06)69473-7
12. Lynes C, McLain AC, Yeung EH, Albert P, Liu J, Boghossian NS. Interpregnancy weight change and adverse maternal outcomes: a retrospective cohort study. *Ann Epidemiol*. 2017;27(10):632-637.e5. doi:10.1016/j.annepidem.2017.09.008
13. Sorbye LM, Skjaerven R, Klungsoyr K, Morken NH. Gestational diabetes mellitus and interpregnancy weight change: A population-based cohort study. *PLoS Med*. 2017;14(8):1-19. doi:10.1371/journal.pmed.1002367
14. Teulings NEWD, Masconi KL, Ozanne SE, Aiken CE, Wood AM. Effect of interpregnancy weight change on perinatal outcomes: Systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2019;19(1). doi:10.1186/s12884-019-2566-2
15. Timmermans YEG, van de Kant KDG, Oosterman EO, et al. The impact of interpregnancy weight change on perinatal outcomes in women and their children: A systematic review and meta-analysis. *Obes Rev*. 2020;21(3). doi:10.1111/obr.12974
16. Nagpal TS, Souza SCS, Moffat M, et al. Does prepregnancy weight change have an effect on subsequent pregnancy health outcomes? A systematic review and meta-analysis. *Obes Rev*. 2022;23(1). doi:10.1111/obr.13324
17. Oteng-Ntim E, Mononen S, Sawicki O, Seed PT, Bick D, Poston L. Interpregnancy weight change and adverse pregnancy outcomes: a systematic review and meta-analysis. *BMJ Open*. 2018;8(6):e018778. doi:10.1136/bmjopen-2017-018778
18. International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy. *Diabetes Care*. 2010;33(3):676-682. doi:10.2337/dc09-1848
19. Yang Y, He R, Zhang N, Li L. Second-Child Fertility Intentions among Urban Women in China: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2023;20(4):3744. doi:10.3390/ijerph20043744
20. Zhu H, Zhao Z, Xu J, et al. The prevalence of gestational diabetes mellitus before and after the implementation of the universal two-child policy in China. *Front Endocrinol (Lausanne)*. 2022;13. doi:10.3389/fendo.2022.960877
21. Wastnedge EAN, Fretwell J, Johns EC, Denison FC, Reynolds RM. First and second pregnancy outcomes in women with class III obesity: An observational cohort study. *Obes Res Clin Pract*. 2021;15(4):357-361. doi:10.1016/j.orcp.2021.05.004
22. Liu J, Song G, Meng T, Zhao G, Guo S. Weight retention at six weeks postpartum and the risk of gestational diabetes mellitus in a second pregnancy. *BMC Pregnancy Childbirth*. 2019;19(1). doi:10.1186/s12884-019-2423-3

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

23. Ku CW, Cheng TS, Ku CO, et al. Distribution and association of interpregnancy weight change with subsequent pregnancy outcomes in Asian women. *Sci Rep*. 2023;13(1). doi:10.1038/s41598-023-31954-5

24. Sparić R, Stojković M, Plešinac J, Pecorella G, Malvasi A, Tinelli A. Advanced maternal age (AMA) and pregnancy: a feasible but problematic event. *Arch Gynecol Obstet*. 2024;310(3):1365-1376. doi:10.1007/s00404-024-07678-w

25. He Y, Ma RCW, David Mcintyre H, et al. Comparing IADPSG and NICE Diagnostic Criteria for GDM in Predicting Adverse Pregnancy Outcomes. *Diabetes Care*. 2022;45(9):2046-2054. doi:10.2337/dc22-0579

26. Chou JS, Packer CH, Mittleman MA, Valent AM. Association of interpregnancy interval and gestational diabetes mellitus. *J Matern Fetal Neonatal Med*. 2022;35(26):10545-10550. doi:10.1080/14767058.2022.2134770

27. Zhu Y, Hedderson MM, Quesenberry CP, Feng J, Ferrara A. Central Obesity Increases the Risk of Gestational Diabetes Partially Through Increasing Insulin Resistance. *Obesity (Silver Spring)*. 2019;27(1):152-160. doi:10.1002/oby.22339

28. *Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines. Weight Gain During Pregnancy: Reexamining the Guidelines. Rasmussen KM, Yaktine AL, Editors. Washington (DC): National Academies Press (U.*

29. Diouf I, Charles MA, Thiebaugeorges O, et al. Maternal weight change before pregnancy in relation to birthweight and risks of adverse pregnancy outcomes. *Eur J Epidemiol*. 2011;26(10):789-796. doi:10.1007/s10654-011-9599-9

30. Whiteman VE, Aliyu MH, August EM, et al. Changes in prepregnancy body mass index between pregnancies and risk of gestational and type 2 diabetes. *Arch Gynecol Obstet*. 2011;284(1):235-240. doi:10.1007/s00404-011-1917-7

31. Bender W, Hirshberg A, Levine LD. Interpregnancy Body Mass Index Changes: Distribution and Impact on Adverse Pregnancy Outcomes in the Subsequent Pregnancy. *Am J Perinatol*. 2019;36(5):517-521. doi:10.1055/s-0038-1670634

32. Knight-Agarwal CR, Williams LT, Davis D, et al. Association of BMI and interpregnancy BMI change with birth outcomes in an Australian obstetric population: A retrospective cohort study. *BMJ Open*. 2016;6(5). doi:10.1136/bmjopen-2015-010667

33. Ehrlich SF, Hedderson MM, Feng J, Davenport ER, Gunderson EP, Ferrara A. Change in body mass index between pregnancies and the risk of gestational diabetes in a second pregnancy. *Obstet Gynecol*. 2011;117(6):1323-1330. doi:10.1097/AOG.0b013e31821aa358

34. Ku CW, Cheng TS, Ku CO, et al. Distribution and association of interpregnancy weight change with subsequent pregnancy outcomes in Asian women. *Sci Rep*. 2023;13(1):1-10. doi:10.1038/s41598-023-31954-5

35. Martínez-Hortelano JA, Cavero-Redondo I, Álvarez-Bueno C, Díez-Fernández A, Hernández-Luengo M, Martínez-Vizcaíno V. Interpregnancy Weight Change and Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Obesity (Silver Spring)*. 2021;29(2):454-464. doi:10.1002/oby.23083

36. Ziauddeen N, Roderick PJ, Macklon NS, Alwan NA. The duration of the interpregnancy interval in multiparous women and maternal weight gain between pregnancies: findings from a UK population-based cohort. *Sci Rep*. 2019;9(1):9175. doi:10.1038/s41598-019-45595-0

37. Thompson M Lou, Ananth C V, Jaddoe VW V, Miller RS, Williams MA. The association of

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

maternal adult weight trajectory with preeclampsia and gestational diabetes mellitus. *Paediatr Perinat Epidemiol*. 2014;28(4):287-296. doi:10.1111/ppe.12128

38. Tano S, Kotani T, Ushida T, et al. Annual Body Mass Index Gain and Risk of Gestational Diabetes Mellitus in a Subsequent Pregnancy. *Front Endocrinol (Lausanne)*. 2022;13(March):1-10. doi:10.3389/fendo.2022.815390

39. Cao J, Xu W, Liu Y, et al. Trends in maternal age and the relationship between advanced age and adverse pregnancy outcomes: a population-based register study in Wuhan, China, 2010–2017. *Public Health*. 2022;206:8-14. doi:10.1016/j.puhe.2022.02.015

40. Li Y, Ren X, He L, Li J, Zhang S, Chen W. Maternal age and the risk of gestational diabetes mellitus: A systematic review and meta-analysis of over 120 million participants. *Diabetes Res Clin Pract*. 2020;162:108044. doi:10.1016/j.diabres.2020.108044

41. Black KI, Schneuer F, Gordon A, Ross GP, Mackie A, Nassar N. Estimating the impact of change in pre-pregnancy body mass index on development of Gestational Diabetes Mellitus: An Australian population-based cohort. *Women and Birth*. 2022;35(6):563-569. doi:10.1016/j.wombi.2021.12.007

42. Lyu J, Sun Y, Ji Y, et al. Optimal Gestational Weight Gain for Women with Gestational Diabetes Mellitus — China, 2011–2021. *China CDC Wkly*. 2023;5(9):189-193. doi:10.46234/ccdcw2023.034

43. Kirkegaard H, Bliddal M, Støvring H, et al. Maternal weight change from prepregnancy to 18 months postpartum and subsequent risk of hypertension and cardiovascular disease in Danish women: A cohort study. *PLoS Med*. 2021;18(4):e1003486. doi:10.1371/journal.pmed.1003486

Figure 1 Flow chart showing inclusion and exclusion in this study *BMI: body mass index; IPWC: interpregnancy weight change.*

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Table 1 The proportion of various IPWCs in different BMI and GDM categories

	IPWC < -3 kg/m^2 [n(%)]	-3 kg/m^2≤IPWC <-2 kg/m^2 [n(%)]	-2 kg/m^2≤IPWC <-1 kg/m^2 [n(%)]	-1 kg/m^2≤IPWC <1 kg/m^2 [n(%)]	1 kg/m^2≤IPWC <2 kg/m^2 [n(%)]	2 kg/m^2≤IPWC <3 kg/m^2 [n(%)]	IPWC ≥3 kg/m^2 [n(%)]
BMI categories in the first pregnancy							
overweight or obese (n=218)	25(11.47)	15(6.88)	21(9.63)	92(42.20)	29(13.30)	19(8.72)	17(7.80)
normal weight (n=1620)	23(1.42)	39(2.41)	141(8.70)	750(46.30)	316(19.51)	192(11.85)	159(9.81)
underweight (n=534)	0(0.00)	3(0.56)	21(3.93)	263(49.25)	141(26.40)	53(9.93)	53(9.93)
GDM in the first pregnancy							
yes (n=265)	10(3.77)	8(3.02)	17(6.42)	118(44.53)	51(19.25)	31(11.70)	30(11.32)
no (n=2107)	38(1.80)	49(2.33)	166(7.88)	987(46.84)	435(20.65)	233(11.06)	199(9.44)
GDM in the second pregnancy							
yes (GDM group) (n=303)	8(2.64)	7(2.31)	17(5.61)	124(40.92)*	69(22.77)	36(11.88)	42(13.86)**
no (non-GDM group) (n=2069)	40(1.93)	50(2.42)	166(8.02)	981(47.41)*	417(20.15)	228(11.02)	187(9.04)**

IPWC: interpregnancy weight change; BMI: body mass index; GDM: gestational diabetes mellitus. *$P<0.05$, **$P<0.01$

For peer review only

bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l'Enseignement Supérieur (ABES). Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

554 Table 2 Univariable analysis of risk factors for the GDM in the second pregnancy

Risk factors	Total (n=2372)	GDM group (n=303)	non-GDM group (n=2069)	Difference of mean or OR	95% CI
maternal age (years，x±s)*	28.27±3.35	29.29±3.53	28.10±3.28	1.184	0.785-1.583
Han nationality[n (%)]*	2255(95.07)	289(95.38)	1966(95.02)	1.081	0.611-1.916
BMI (kg/m^2)*	20.49±2.64	21.33±3.02	20.36±2.55	0.963	0.604-1.321
continuous IPWC [kg/m^2 (interquartile range)]	0.725(-0.240-1.770)	0.970(-0.150-2.110)	0.680(-0.250-1.730)	0.221	0.000-0.442
BMI in the second pregnancy (kg/m^2)	21.27±2.90	22.30±3.31	21.12±2.81	1.184	0.791-1.576
IPI [months (interquartile range)]	31.68(22.50-43.56)	36.16(26.07-48.53)	30.95(22.25-46.25)	4.398	2.579-6.218
ART [n (%)]*	120(5.06)	20(6.60)	100(4.83)	1.392	0.847-2.285
GDM [n (%)]*	265(11.17)	126(41.58)	139(6.72)	9.884	7.425-13.157
HDCP [n (%)]*	81(3.41)	20(6.60)	61(2.95)	2.326	1.383-3.914
hypothyroidism [n (%)]*	132(5.56)	14(4.62)	118(5.70)	0.801	0.454-1.413
hyperthyroidism [n (%)]*	18(0.76)	2(0.66)	16(0.77)	0.853	0.195-3.726
APS [n (%)]*	4(0.17)	0(0.00)	4(0.19)	-	-
SLE [n (%)]*	12(0.51)	0(0.00)	12(0.58)	-	-
PPH [n (%)]*	42(1.77)	8(2.64)	34(1.64)	1.623	0.744-3.540
PCOS [n (%)]*	6(0.25)	2(0.66)	4(0.19)	3.430	0.626-18.808
CS [n (%)]*	735(30.99)	125(41.25)	610(29.48)	1.680	1.311-2.151
PTB [n (%)]*	131(5.52)	23(7.59)	108(5.22)	1.492	0.935-2.380
macrosomia [n (%)]*	99(4.17)	18(5.94)	81(3.91)	1.550	0.916-2.622
male newborn [n (%)]*	1181(49.79)	148(48.84)	1033(49.93)	0.958	0.752-1.219

555 * in the first pregnancy; BMI: body mass index; IPWC: interpregnancy weight change; IPI: interpregnancy interval;
556 ART: assisted reproductive technology; GDM: gestational diabetes mellitus; HDCP: hypertensive disorder
557 complicating pregnancy; APS: antiphospholipid syndrome; SLE: systemic lupus erythematosus; PPH: postpartum
558 hemorrhage; PCOS: polycystic ovary syndrome; CS:cesarean section; PTB: preterm birth; OR: Odds Ratio; CI:
559 confidence interval.
560
561
562 Table 3 The effect of IPWC categories on the GDM in the second pregnancy in univariable and
563 multivariable analysis

variables	non-adjusted		model 1*		model 2 #	
	OR	95% CI	adjusted OR	95% CI	adjusted OR	95% CI
IPWC < -3 kg/m^2	1.582	0.724-3.458	0.830	0.326-2.114	0.796	0.324-1.955
-3 kg/m^2≤IPWC <-2 kg/m^2	1.108	0.491-2.497	0.831	0.341-2.023	0.833	0.346-2.004
-2 kg/m^2≤IPWC <-1 kg/m^2	0.810	0.475-1.380	0.826	0.466-1.463	0.772	0.438-1.364
-1 kg/m^2≤IPWC <1 kg/m^2	reference	reference	reference	reference	reference	reference
1 kg/m^2≤IPWC <2 kg/m^2	1.309	0.954-1.795	**1.414**	**1.001-1.997**	**1.443**	**1.026-2.031**
2 kg/m^2≤IPWC <3 kg/m^2	1.249	0.839-1.860	1.231	0.792-1.912	1.221	0.793-1.880
IPWC ≥3 kg/m^2	**1.777**	**1.211-2.607**	**1.794**	**1.170-2.749**	**1.818**	**1.194-2.767**

564 * adjusted by BMI of the first trimester, continuous interpregnancy interval (IPI), maternal age, GDM, hypertensive
565 disorder complicating pregnancy (HDCP), macrosomia, preterm delivery, and cesarean delivery in the first
566 pregnancy; # adjusted by BMI of the first trimester and GDM in the first pregnancy; IPWC: interpregnancy weight
567 change; GDM: gestational diabetes mellitus; OR: Odds Ratio; CI: confidence interval.
568
569

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Table 4 The effect of continuous IPWC value on the GDM in the second pregnancy in total and stratified subgroups

Population included	non-adjusted		model 1*		model 2 #	
	OR	95% CI	adjusted OR	95% CI	adjusted OR	95% CI
total (n=2372)	1.067	1.000-1.139	**1.105**	**1.029-1.186**	**1.111**	**1.038-1.190**
IPI⩾36 months (n=947)	1.069	0.970-1.180	1.091	0.984-1.210	1.097	0.990-1.215
IPI < 36 months (n=1425)	1.055	0.966-1.154	**1.118**	**1.014-1.232**	**1.116**	**1.015-1.227**
maternal age⩾35 years old $ (n=86)	1.034	0.786-1.360	1.075	0.754-1.533	1.052	0.776-1.427
maternal age < 35 years $ (n=2286)	**1.080**	**1.010-1.156**	**1.110**	**1.032-1.194**	**1.120**	**1.043-1.202**
GDM $ (n=265)	1.034	0.786-1.360	1.094	0.967-1.239	1.099	0.974-1.241
without GDM $ (n=2107)	**1.096**	**1.008-1.191**	**1.116**	**1.024-1.216**	**1.117**	**1.028-1.214**
overweight or obese $ (n=218)	1.079	0.943-1.235	1.093	0.941-1.271	1.082	0.938-1.248
normal weight $ (n=1620)	**1.096**	**1.011-1.188**	**1.119**	**1.024-1.222**	**1.126**	**1.033-1.228**
underweight $ (n=534)	1.126	0.952-1.332	1.084	0.882-1.331	1.105	0.924-1.322

* adjusted by continuous IPWC value, BMI of the first trimester, continuous interpregnancy interval (IPI), maternal age, GDM, hypertensive disorder complicating pregnancy (HDCP), macrosomia, preterm delivery, and cesarean delivery in the first pregnancy; # adjusted by BMI of the first trimester and GDM in the first pregnancy; $ in the first pregnancy.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Table 5 Adjusted OR values of IPWC categories for the GDM risk in the second pregnancy in stratified analysis

Population included	adjusted OR (95% CI)				
	IPWC < -3 kg/m^2	-3 kg/m^2≤IPWC <-2 kg/m^2	-2 kg/m^2≤IPWC <-1 kg/m^2	-1 kg/m^2≤IPWC <1 kg/m^2	1 kg/m^2≤IPWC <2 kg/m^2
Model 1[a]					
IPI≥36 months (n=947)	1.174 (0.335-4.114)	1.117 (0.317-3.930)	0.677 (0.277-1.658)	reference	1.370 (0.844-2.225)
IPI < 36 months (n=1425)	0.600 (0.139-2.589)	0.679 (0.185-2.485)	1.007 (0.479-2.115)	reference	1.488 (0.906-2.443)
maternal age≥35 years old [#] (n=86)	1.907 (0.058-62.300)	- [*]	3.559 (0.549-23.055)	reference	3.710 (0.760-18.107)
maternal age < 35 years [#] (n=2286)	0.884 (0.331-2.359)	1.014 (0.413-2.493)	0.748 (0.403-1.389)	reference	1.396 (0.975-1.999)
GDM[#] (n=265)	0.670 (0.167-2.680)	0.597 (0.133-2.675)	0.646 (0.218-1.910)	reference	1.163 (0.589-2.297)
Without GDM[#] (n=2107)	1.008 (0.288-3.523)	0.987 (0.333-2.925)	0.925 (0.473-1.807)	reference	**1.537 (1.027-2.301)**
overweight or obese [#] (n=218)	0.649 (0.179-2.356)	2.125 (0.517-8.744)	0.595 (0.138-2.559)	reference	0.993 (0.295-3.339)
Normal weight [#] (n=1620)	1.257 (0.320-4.931)	0.397 (0.108-1.459)	0.93 (0.491-1.763)	reference	1.330 (0.870-2.032)
underweight [#] (n=534)	- [*]	- [*]	- [*]	reference	1.703 (0.813-3.567)
Model 2[b]					
IPI≥36 months (n=947)	1.107 (0.321-3.816)	1.009 (0.291-3.498)	0.620 (0.255-1.508)	reference	1.331 (0.823-2.153)
IPI < 36 months (n=1425)	0.526 (0.132-2.092)	0.687 (0.188-2.502)	0.928 (0.440-1.956)	reference	1.442 (0.883-2.357)
maternal age≥35 years old [#] (n=86)	0.803 (0.046-13.873)	- [*]	1.597 (0.310-8.218)	reference	2.144 (0.544-8.446)
maternal age < 35 years [#] (n=2286)	0.843 (0.326-2.177)	0.994 (0.409-2.412)	0.703 (0.379-1.301)	reference	**1.438 (1.008-2.052)**
GDM[#] (n=265)	0.694 (0.178-2.714)	0.616 (0.140-2.714)	0.582 (0.200-1.691)	reference	1.224 (0.627-2.391)
Without GDM[#] (n=2107)	0.831 (0.244-2.832)	0.981 (0.339-2.834)	0.871 (0.449-1.689)	reference	**1.542 (1.036-2.296)**
overweight or obese [#] (n=218)	0.736 (0.218-2.487)	2.490 (0.646-9.590)	0.691 (0.164-2.913)	reference	1.224 (0.395-3.796)
normal weight [#] (n=1620)	1.038 (0.274-3.925)	0.386 (0.107-1.400)	0.845 (0.446-1.600)	reference	1.314 (0.863-2.003)
underweight [#] (n=534)	- [*]	- [*]	- [*]	reference	1.930 (0.954-3.905)

[a] adjusted by IPWC categories, BMI of the first trimester, continuous interpregnancy interval (IPI), maternal age, GDM, hypertensive disorder complicating pregnancy (HDCP), macrosomia, preterm delivery, and cesarean delivery in the first pregnancy; [b] adjusted by BMI of the first trimester and GDM in the first pregnancy; [*] OR value can not be calculated because there were no cases of GDM in the second pregnancy in this subgroup; [#] in the first

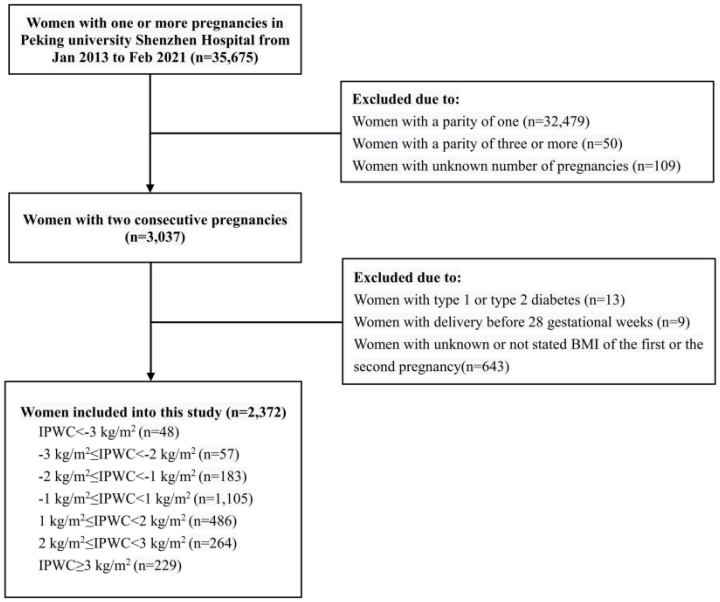
For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Supérieur (ABES) .

pregnancy. IPWC: interpregnancy weight change; IPI: interpregnancy interval; GDM: gestational diabetes mellitus; OR: Odds Ratio; CI: confidence interval.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .



209x296mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table S1 Collinearity analysis of the independent variables

variables	tolerance	VIF
IPWC	0.957	1.044
IPI	0.139	7.219
Maternal age in the first pregnancy	0.021	47.898
Maternal age in the second pregnancy	0.018	55.443
BMI of the first trimester and GDM in the first pregnancy	0.928	1.077
BMI of the first trimester and GDM in the second pregnancy*	0.000	-

* this variable was excluded during the analysis; IPWC: interpregnancy weight change; IPI: interpregnancy interval; VIF: variance inflation factor.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

Table S2 The OR value changes of IPWC effect on the GDM in the second pregnancy after adjusted by different kinds of independent variable

	IPWC < -3 kg/m2	-3 kg/m2≤ IPWC <-2 kg/m2	-2 kg/m2≤ IPWC <-1 kg/m2	-1 kg/m2 ≤IPWC <1 kg/m2	1 kg/m2≤ IPWC <2 kg/m2	2 kg/m2≤ IPWC <3 kg/m2	IPWC ≥3 kg/m2
Non-adjusted OR value	1.582	1.108	0.81	reference	1.309	1.249	1.777
OR adjusted by IPI	1.598	1.142	0.832	reference	1.288	1.253	1.743
Percentage of the OR change	1.01%	3.07%	2.72%	-	-1.60%	0.32%	-1.91%
OR adjusted by maternal age [a]	1.643	1.067	0.816	reference	1.346	1.321	1.862
Percentage of the OR change	3.86%	-3.70%	0.74%	-	2.83%	5.76%	4.78%
OR adjusted by nationality	1.581	1.109	0.808	reference	1.311	1.246	1.776
Percentage of the OR change	-0.06%	0.09%	-0.25%	-	0.15%	-0.24%	-0.06%
OR adjusted by newborn sex [a]	1.578	1.109	0.809	reference	1.309	1.246	1.774
Percentage of the OR change	-0.25%	0.09%	-0.12%	-	0.00%	-0.24%	-0.17%
OR adjusted by GDM [a]	1.172	0.982	0.836	reference	1.375	1.238	1.782
Percentage of the OR change	**-25.92%**	**-11.37%**	3.21%	-	5.04%	-0.88%	0.28%
OR adjusted by HDCP [a]	1.569	1.083	0.809	reference	1.306	1.242	1.775
Percentage of the OR change	-0.82%	-2.26%	-0.12%	-	-0.23%	-0.56%	-0.11%
OR adjusted by macrosomia [a]	1.566	1.092	0.809	reference	1.316	1.248	1.757
Percentage of the OR change	-1.01%	-1.44%	-0.12%	-	0.53%	-0.08%	-1.13%
OR adjusted by preterm birth [a]	1.59	1.089	0.811	reference	1.299	1.242	1.787
Percentage of the OR change	0.51%	-1.71%	0.12%	-	-0.76%	-0.56%	0.56%
OR adjusted by CS [a]	1.566	1.115	0.798	reference	1.319	1.252	1.771
Percentage of the OR change	-1.01%	0.63%	-1.48%	-	0.76%	0.24%	-0.34%
OR adjusted by BMI [a]	0.906	0.837	0.718	reference	1.398	1.229	1.835
Percentage of the OR change	**-42.73%**	**-24.46%**	**-11.36%**	-	6.8%	-1.6%	3.26%
OR adjusted by maternal age in the second pregnancy	1.641	1.06	0.825	reference	1.336	1.326	1.869
Percentage of the OR change	3.73%	-4.33%	1.85%	-	2.06%	6.16%	5.18%

[a] in the first pregnancy; BMI: body mass index; IPWC: interpregnancy weight change; IPI: interpregnancy interval; GDM: gestational diabetes mellitus; HDCP: hypertensive disorder complicating pregnancy; CS:cesarean section; PTB: preterm birth; OR: odds ratio.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Table S3 Adjusted OR values of five IPWC categories for the GDM risk in the second pregnancy in total and in stratified analysis

	adjusted OR (95% CI)*				
	IPWC <-1 kg/m²	-1 kg/m²≤IPWC <1 kg/m²	1 kg/m²≤IPWC <2 kg/m²	2 kg/m²≤IPWC <3 kg/m²	IPWC ≥3 kg/m²
In total (n=2372)	0.790(0.502-1.243)	reference	**1.443(1.026-2.031)**	1.221(0.793-1.880)	**1.818(1.194-2.768)**
IPI⩾36 months (n=947)	0.786(0.400-1.544)	reference	1.334(0.824-2.159)	1.514(0.850-2.697)	1.422(0.758-2.669)
IPI < 36 months (n=1425)	0.786(0.421-1.469)	reference	1.438(0.880-2.348)	0.839(0.421-1.671)	**2.208(1.249-3.902)**
maternal age⩾35 years old#(n=86)	0.886(0.211-3.727)	reference	2.147(0.548-8.403)	-[a]	1.614(0.228-11.410)
maternal age < 35 years# (n=2286)	0.789(0.488-1.273)	reference	**1.439(1.009-2.054)**	1.313(0.848-2.033)	**1.851(1.201-2.851)**
GDM# (n=265)	0.619(0.280-1.369)	reference	1.226(0.628-2.396)	0.914(0.409-2.042)	1.723(0.752-3.946)
Without GDM# (n=2107)	0.886(0.512-1.533)	reference	**1.542(1.036-2.296)**	1.373(0.839-2.247)	**1.867(1.140-3.056)**
overweight or obese # (n=218)	0.991(0.411-2.390)	reference	1.202(0.392-3.687)	1.611(0.485-5.357)	1.814(0.521-6.315)
normal weight # (n=1620)	0.749(0.428-1.309)	reference	1.314(0.863-2.000)	1.256(0.759-2.078)	**1.929(1.170-3.183)**
underweight # (n=534)	-[a]	reference	1.930(0.954-3.905)	0.722(0.197-2.656)	1.471(0.548-3.946)

[a] OR value can not be calculated because there were no cases of GDM in the second pregnancy in this subgroup. # in the first pregnancy; * adjusted by BMI of the first trimester and GDM in the first pregnancy;IPWC: interpregnancy weight change; IPI: interpregnancy interval; GDM: gestational diabetes mellitus; OR: Odds Ratio; CI: confidence interval.

For peer review only

bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Supérieur (ABES)

d by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table S4 The interaction effect of IPWC categories with stratified factors for the GDM risk in the second pregnancy

variables	adjusted OR[#]	95% CI[#]
IPWC categories interacted with IPI categories		
IPWC < -3 kg/m^2 interacted with IPI ≥36 months	1.649	0.272–10.006
-3 kg/m^2≤IPWC <-2 kg/m^2 interacted with IPI ≥36 months	1.313	0.220–7.822
-2 kg/m^2≤IPWC <-1 kg/m^2 interacted with IPI ≥36 months	0.635	0.199–2.027
-1 kg/m^2≤IPWC <1 kg/m^2 interacted with IPI ≥36 months	reference	reference
1 kg/m^2≤IPWC <2 kg/m^2 interacted with IPI ≥36 months	0.956	0.482–1.898
2 kg/m^2≤IPWC <3 kg/m^2 interacted with IPI ≥36 months	1.788	0.727–4.396
IPWC ≥3 kg/m^2 interacted with IPI ≥36 months	0.655	0.279–1.535
IPWC categories interacted with maternal age ≥35 years old*		
IPWC < -3 kg/m^2 interacted with maternal age ≥35 years old*	0.458	0.026–8.014
-3 kg/m^2≤IPWC <-2 kg/m^2 interacted with maternal age ≥35 years old* $	—[a]	—[a]
-2 kg/m^2≤IPWC <-1 kg/m^2 interacted with maternal age ≥35 years old*	2.236	0.365–13.706
-1 kg/m^2≤IPWC <1 kg/m^2 interacted with maternal age ≥35 years old*	reference	reference
1 kg/m^2≤IPWC <2 kg/m^2 interacted with maternal age ≥35 years old*	1.514	0.345–6.647
2 kg/m^2≤IPWC <3 kg/m^2 interacted with maternal age ≥35 years old* $	—[a]	—[a]
IPWC ≥3 kg/m^2 interacted with maternal age ≥35 years old*	1.206	0.159–9.122
IPWC categories interacted with GDM*		
IPWC < -3 kg/m^2 interacted with GDM*	0.932	0.158–5.496
-3 kg/m^2≤IPWC <-2 kg/m^2 interacted with GDM*	0.651	0.106–4.007
-2 kg/m^2≤IPWC <-1 kg/m^2 interacted with GDM*	0.681	0.195–2.381
-1 kg/m^2≤IPWC <1 kg/m^2 interacted with GDM*	reference	reference
1 kg/m^2≤IPWC <2 kg/m^2 interacted with GDM*	0.779	0.359–1.687
2 kg/m^2≤IPWC <3 kg/m^2 interacted with GDM*	0.670	0.260–1.727
IPWC ≥3 kg/m^2 interacted with GDM*	0.917	0.351–2.398
IPWC categories interacted with the BMI categories of the first trimester*		
IPWC < -3 kg/m^2 interacted with BMI < 18.5 kg/m^{2*} $	—[a]	—[a]
-3 kg/m^2≤IPWC <-2 kg/m^2 interacted with BMI < 18.5 kg/m^{2*} $	—[a]	—[a]
-2 kg/m^2≤IPWC <-1 kg/m^2 interacted with BMI < 18.5 kg/m^{2*} $	—[a]	—[a]
-1 kg/m^2≤IPWC <1 kg/m^2 interacted with BMI < 18.5 kg/m^{2*}	reference	reference
1 kg/m^2≤IPWC <2 kg/m^2 interacted with BMI < 18.5 kg/m^{2*}	1.465	0.646–3.323
2 kg/m^2≤IPWC <3 kg/m^2 interacted with BMI < 18.5 kg/m^{2*}	0.550	0.136–2.222
IPWC ≥3 kg/m^2 interacted with BMI < 18.5 kg/m^{2*}	0.770	0.255–2.328
IPWC < -3 kg/m^2 interacted with BMI ≥ 24 kg/m^{2*}	0.572	0.095–3.452
-3 kg/m^2≤IPWC <-2 kg/m^2 interacted with BMI ≥ 24 kg/m^{2*}	5.663	0.897–35.759
-2 kg/m^2≤IPWC <-1 kg/m^2 interacted with BMI ≥ 24 kg/m^{2*}	0.741	0.153–3.603
-1 kg/m^2≤IPWC <1 kg/m^2 interacted with BMI ≥ 24 kg/m^{2*}	reference	reference
1 kg/m^2≤IPWC <2 kg/m^2 interacted with BMI ≥ 24 kg/m^{2*}	0.955	0.283–3.217
2 kg/m^2≤IPWC <3 kg/m^2 interacted with BMI ≥ 24 kg/m^{2*}	1.260	0.330–4.805
IPWC ≥3 kg/m^2 interacted with BMI ≥ 24 kg/m^{2*}	0.953	0.242–3.744

* in the first pregnancy; # adjusted by BMI of the first trimester and GDM in the first pregnancy; [a] OR value

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

can not be calculated because there were no cases of GDM in the second pregnancy in this subgroup.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Table S5 The interaction effect of continuous IPWC value with stratified factors for the GDM risk in the second pregnancy

variables	adjusted OR[#]	95% CI[#]
Continuous IPWC interacted with continuous IPI	1. 001	0. 997–1. 005
Continuous IPWC interacted with maternal age[*]	0. 996	0. 977–1. 016
Continuous IPWC interacted with GDM[*]	0. 978	0. 847–1. 128
Continuous IPWC interacted with continuous BMI in the first trimester	1. 001	0. 980–1. 022

[*] in the first pregnancy; [#] adjusted by BMI of the first trimester and GDM in the first pregnancy.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

BMJ Open

The impact of interpregnancy weight change on the risk of gestational diabetes mellitus during a second pregnancy in Chinese population：a retrospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-084282.R2
Article Type:	Original research
Date Submitted by the Author:	23-Dec-2024
Complete List of Authors:	Yang, Ao; Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital; Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center; Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases Wang, Ying; Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital; Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center; Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases Liu, Yuzhen; Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Center of Obstetrics and Gynecology; Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center; Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases Yang, Juan; Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital; Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center; Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases Xu, Chang; Intelligent Hospital Research Academy, Peking University Shenzhen Hospital Zhong, Shilin; Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital; Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center; Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases
Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Obstetrics and gynaecology
Keywords:	Diabetes in pregnancy < DIABETES & ENDOCRINOLOGY, OBSTETRICS, Weight Gain, Maternal medicine < OBSTETRICS, Risk Factors

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

The impact of interpregnancy weight change on the risk of gestational diabetes mellitus during a second pregnancy in Chinese population：a retrospective cohort study

Ao Yang[1,2,3] *, Ying Wang[1,2,3] *, Yuzhen Liu[1,2,3] *, Juan Yang[1,2,3], Chang Xu[4], Shilin Zhong[1,2,3]

[1]Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China.
[2]Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen, Guangdong, China.
[3]Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases, Shenzhen, Guangdong, China.
[4]Intelligent Hospital Research Academy, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China.
*Ao Yang, Ying Wang and Yuzhen Liu contributed equally to this article.
Correspondence
Shilin Zhong, Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, 1120 Lianhua Road, Shenzhen 518036, Guangdong, China.
Email: zhongshilin2013@163.com

Abstract

Objectives This study aimed to investigate the impact of interpregnancy weight changes (IPWC) on the gestational diabetes mellitus (GDM) in the second pregnancy.
Design A retrospective cohort study.
Setting Data were collected in Peking University Shenzhen Hospital from 2013 Jan to 2021 Feb.
Participants Women who had two consecutive singleton deliveries after 28 gestational weeks (N=2372).
Outcomes The GDM in the second pregnancy (s-GDM).
Methods: IPWC was defined as the change in BMI between the first trimester of the second pregnancy and that of the first pregnancy, categorized into four groups with -1 kg/m² to <1 kg/m² as the reference. Adjusted odds ratios (aORs) with 95% CIs attained from multivariable logistic regression were used to assess the association between IPWC and s-GDM, in both total subjects and stratified subgroups.
Results: In the overall analysis, s-GDM was found to be significantly associated with IPWC value (aOR 1.111; 95%CI 1.038-1.190) and an IPWC category of ≥ 3 kg/m² (aOR 1.821; 95%CI 1.197-2.772). In the stratified analysis, the significant association between IPWC ≥3 kg/m² and s-GDM was evident only in the subgroups of an inter-pregnancy interval (IPI) of less than 36 months (aOR 2.210, 95%CI 1.251-3.904), under the age of 35 (aOR 1.854, 95%CI 1.204-2.857), non-diabetic status in the first pregnancy (f-ND) (aOR 1.872, 95%CI 1.143-3.065), and those with normal weight in the first pregnancy (f-NW) (aOR 1.936, 95%CI 1.174-3.193). The significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

association between IPWC value and s-GDM was also showed only in these subgroups ($P< 0.05$). In f-DN subgroup, even an IPWC category of 1 kg/m² to <3 kg/m² was significantly associated with s-GDM (aOR 1.486, 95%CI 1.044-2.117). IPWC < -1 kg/m² was not significantly associated with s-GDM either in the overall analysis or in the stratified analysis ($P >0.05$).

Conclusion: An IPWC of 3 kg/m² or higher may increase the risk of s-GDM, particularly among women with an IPI less than 36 months, those under 35 years old, non-diabetic individuals, or those with normal weight during their first pregnancy. The potential influence of prior GDM on the relationship between IPWC and s-GDM warrants further investigation.

Keywords gestational diabetes mellitus, interpregnancy weight change, risk factor, maternal age, interpregnancy interval

Strength and limitations of this study

► The association between IPWC and s-GDM was examined in a cohort of 2,372 cases involving consecutive singleton births in China.

► Both the IPWC value and an IPWC ≥3 kg/m² were significantly associated with s-GDM, as demonstrated by two multivariable logistic regression models. Stratified analysis revealed that these associations were present only in women with IPI < 36 months, maternal age < 35 years old, without previous GDM, and those with normal weight during their first pregnancy.

► This study did not reveal a significant association between IPWC < -1 kg/m² and a reduced risk of s-GDM.

► The main limitation is the retrospective design, and the data of diet, family history of diabetes, and gestational weight gain during the first pregnancy, were not included in the analysis.

► The sample size for certain subgroups is relatively small.

INTRODUCTION

Gestational diabetes (GDM) is a type of diabetes that develops during pregnancy. In China, the prevalence of GDM is as high as 14.8%[1],leading to adverse consequences for both the mother and the fetus. Consequently, it is crucial to implement preventive actions to effectively manage the occurrence of diabetes in advance, yielding significant clinical relevance.

The occurrence of GDM is influenced by various factors, such as weight[2], diet[3], maternal age[4], exercise, and genetics[5]. Weight is particularly significant in relation to GDM development. Excessive weight gain during pregnancy proves to be a major risk factor for GDM[6,7]. Research conducted in China highlights the close relationship between pre-pregnancy weight and GDM[8].

Several studies indicate a significant correlation between interpregnancy weight changes (IPWC) and GDM in the second pregnancy (s-GDM) [9, 10, 11, 12, 13]. However, there is no consensus on the precise impact of IPWC on the risk of s-GDM. In 2019-2021, systematic analyses by Teulings et al. [14], Timmermans et al. [15], and Nagpal et al. [16] confirmed the positive association between IPWC and s-GDM risk. Nevertheless, these studies did not find that weight loss between pregnancies reduced the s-GDM risk. Conversely, Oteng-Ntim et al.'s systematic review[17] suggested the protective effect of reducing IPWC on s-GDM. Timmermans et al. [15] identified that an IPWC of 1 to 3 kg/m² correlates with an odds ratio (OR) of 1.64 (95% CI 1.28-2.11) for s-GDM, and IPWC of ≥3 kg/m² with an OR of 2.42 (95% CI 1.62-3.62). However, three out of five studies gathered data prior to 2010, and the remaining two included some pre-2010 cases. Given

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

that current GDM diagnostic criteria in China were recommended by the IADPSG in 2010[18], these studies' applicability to the Chinese population warrants reevaluation. Furthermore, most existing studies lack stratified analyses based on interpregnancy interval (IPI) or maternal age. Variations in study populations could lead to differing results, and there is a notable absence of large-scale studies within the Chinese demographic. Consequently, further investigation among the Chinese population is essential.

Since 2016, China's two-child policy has been implemented to stimulate a rise in fertility levels. It has been found that 37% of couples have expressed intentions to have a second child [19]. A higher proportion of advanced maternal age (>30 years) and multiparity have increased the risk of GDM[20]. The interpregnancy period is a critical time of weight management and health improvement to reduce the risk of s-GDM [21,22]. Regardless of whether they have had diabetes in their first pregnancy, both women and their physicians are interested in determining the ideal weight management target to minimize the risk of GDM in future pregnancies. Therefore, we conducted a single-center, retrospective study in China to analyze the impact of weight change during two pregnancies on the risk of GDM in the second pregnancy (s-GDM).

MATERIALS ADN METHODS

Study design and population

We conducted a retrospective cohort study involving participants who had two consecutive singleton deliveries after the 28th week of gestation at Peking University Shenzhen Hospital from January 2013 to February 2021. The study excluded women with multiple pregnancies, parity of one, parity of three or more, deliveries before 28 weeks of gestation, missing BMI data, type 1 or type 2 diabetes, and those with unstated BMI for either of their pregnancies. The Medical Ethics Committee of Peking University Shenzhen Hospital approved the study protocol (#2023-103). Participants were categorized into the GDM group (s-GDM) and the non-diabetic status group (s-ND) based on their GDM status in the second pregnancy.

Patient and Public Involvement statement

None

Definitions of the variables and outcome

In this study involving two consecutive pregnancies, we designated the earlier pregnancy as "the first pregnancy" and the latter as "the second pregnancy". The primary variable examined was interpregnancy weight change (IPWC), defined as the difference in body mass index (BMI) between the first trimester of the second pregnancy and that of the first pregnancy [23]. IPWC, expressed in BMI units (kg/m^2), was categorized into four groups: <-1 kg/m^2, -1 kg/m^2 to <1 kg/m^2 (considered as stable BMI and used as a reference), 1 kg/m^2 to <3 kg/m^2, and ≥3 kg/m^2 [24]. BMI level in the first pregnancy (f-BMI) was classified into four categories: underweight (f-UW) (<18.5 kg/m^2), normal weight (f-NW) (18.5 kg/m^2 to <24.0 kg/m^2), and overweight or obese (f-OB) (≥24.0 kg/m^2). The interpregnancy interval (IPI) was defined as the duration in months between the end of one pregnancy and the start of the next, calculated by subtracting the gestational age at the second delivery from the interval between the delivery dates of two

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

consecutive pregnancies [23]. Advanced maternal age (AMA) was described as being 35 years or older [25], and young maternal age (YMA) was defined as the age less than 35 years old.

The primary outcome of the study was the GDM in the second pregnancy (s-GDM). Throughout the entire study period, GDM was diagnosed using the IADPSG criteria[26], which involved a 75-gram oral glucose tolerance test. According to these criteria, a diagnosis of GDM was made if the serum blood glucose levels were ≥5.1 mmol/L at 0 hour, and/or ≥10.0 mmol/L at 1 hour, and/or ≥8.5 mmol/L at 2 hours, between 24-28 weeks of gestation.

Data collection

The data for this study were obtained from the delivery records within the hospital information system and the Shenzhen maternal and child health management system. The collected data include the information of previous pregnancy, such as, maternal age, parity, date and gestational weeks of delivery, delivery mode, occupation, medical payment method, ethnicity, marital status, sex of newborn, birth weight, BMI (f-BMI), complications or comorbidities including GDM in the first pregnancy (f-GDM), hypertensive disorder complicating pregnancy (HDCP), postpartum hemorrhage (PPH), thyroid disease, systemic lupus erythematosus (SLE), and preterm birth (PTB), et al., and the information of the second pregnancy, such as body mass index (s-BMI) and GDM status (s-GDM).

Statistical method

The data analysis was performed using SPSS 24.0 statistical software (IBM, Armonk, NY, USA). Categorical variables were presented as n (%) and compared using the Chi-square test. Normally distributed variables were presented as mean ± standard deviation and compared using the student's *t*-test. Non-normally distributed variables were presented as median (interquartile range; IQR) and compared using the Mann-Whitney *U* test. Two multivariable regression models were used to assess the association between IPWC and s-GDM. Model 1 included the covariates with significant difference ($P < 0.1$) in univariable analysis and variance inflation factor (VIF) < 10 in collinearity assessment. Model 2 only included the covariates which altered the odds ratio (OR) of IPWC on s-GDM by more than 10%. Stratified analysis was performed within specific subgroups categorized by IPI (≥36 months, < 36 months [27]), and the variables of previous pregnancy, such as maternal age (f-AMA, f-YMA), GDM status (f-GDM, f-ND), and BMI level (f-OB, f-NW and f-UW). Additionally, this study separately analyzed the interaction between IPWC value and categories with these four stratification factors. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Baseline characteristics of the subjects

A total of 35,675 participants who had experienced at least one pregnancy at Peking University Shenzhen Hospital were recorded between January 2013 and February 2021. After disqualifying 33,303 participants based on the exclusion criteria, a final cohort of 2,372 participants who had undergone two consecutive single deliveries were included (Figure 1).

During the first pregnancy, the participants' average age was 28.25 ± 3.33 years, with a mean BMI of 20.48 ± 2.64 kg/m² and an average delivery gestational age of 38.82 ± 1.53 weeks. Instances of f-GDM occurred in 265 cases (11.17%). The prevalence of f-GDM among subjects

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

with f-UW, f-NW, and f-OB was 8.61% (46/534), 10.19% (165/1620), and 24.77% (54/218), respectively.

The median IPWC for all participants was 0.725 kg/m² (P25: -0.240 kg/m²; P75: 1.770 kg/m²). Figure 2A illustrates the distribution of four IPWC categories. Subjects with an IPI of 36 months or more had a higher proportion of IPWC ranging from 1 to < 3 kg/m² ($P = 0.001$) and a lower proportion of stable IPWC compared to those with an IPI of less than 36 months ($P = 0.008$, Figure 2B). There was no significant difference in the proportions of all four IPWC categories between those with and without f-GDM ($P > 0.05$, Figure 2C). Compared to women with f-UW, a larger percentage of women with f-OB had an IPWC of less than -1 kg/m² ($P < 0.001$, Figure 2D), while a smaller percentage had an IPWC of 2-3 kg/m² ($P < 0.001$, Figure 2D).

During the second pregnancy, the participants had an average age of 31.15 ± 3.57 years. The mean BMI was 21.27 ± 2.90 kg/m², and the average gestational age at delivery was 38.54 ± 1.45 weeks. Notably, 303 participants, accounting for 12.77% of the total, were diagnosed with s-GDM.

Comparison of IPWC and other risk factors between s-GDM and s-ND groups

In the s-GDM group, the IPWC value, maternal age, f-BMI, s-BMI, and IPI were all significantly higher compared to the s-ND group ($P < 0.01$, Table 1). Moreover, the percentage of participants with IPWC ⩾ 3kg/m², f-GDM, f-HDCP, f-CS, f-AMA, f-OB, and IPI ⩾ 36 months was notably greater in the s-GDM group than in the s-ND group ($P < 0.01$, Table 1). Conversely, the proportion of subjects with a stable IPWC (-1 kg/m² to <1 kg/m²) and f-UW was significantly lower in the s-GDM group than in the s-ND group ($P < 0.05$, Table 1).

The effect of IPWC on s-GDM in total subjects

Following univariable and collinearity analyses (Supplementary Table 1), variables such as IPI, f-BMI, maternal age (f-MA), f-GDM, f-HDCP, f-macrosomia, f-PTB, and f-CS were included in Model 1. Subsequently, f-BMI and f-GDM were incorporated into Model 2 due to their notable impact on the effect of IPWC in bivariable analyses. In both adjusted models (Model 1 and Model 2), the IPWC value was significantly positively associated with s-GDM, while this association was marginal in the unadjusted model (P=0.05, Table 2).

In both unadjusted and adjusted models, an IPWC of ⩾3 kg/m² was independently linked to an increased risk of s-GDM compared to the reference IPWC (Table 2). Moreover, Model 2 revealed that an IPWC ranging from 1 kg/m² to <3 kg/m² was also linked to a heightened risk of s-GDM. In contrast, other IPWC categories, such as IPWC < -1 kg/m², demonstrated no significant association with s-GDM (Table 2).

The effect of IPWC on s-GDM in stratified analysis

In alignment with the unadjusted model, both Model 1 and Model 2 demonstrated a significant association between the IPWC value and an increased risk of s-GDM within the f-YMA, f-ND, and f-NW subgroups (Table 3). Furthermore, both Model 1 and Model 2 indicated a significant correlation between the IPWC value and s-GDM in subgroups with an IPI of less than 36 months, whereas this relationship was not observed in the unadjusted model (Table 3). However, the IPWC value did not correlate significantly with s-GDM in subgroup of IPI ⩾ 36 months, as well as in the f-AMA, f-GDM, f-OB, or f-UW subgroups (Table 3). Additionally, there was no significant interaction between IPWC value and the four stratification factors ($P > 0.05$, Table 3).

IPWC ⩾ 3 kg/m² was significantly correlated with an increased risk of s-GDM for

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

individuals with an IPI of less than 36 months, f-YMA, f-DN, and f-NW, across both unadjusted models and adjusted models (Model 1 and Model 2) (Table 4). Furthermore, both unadjusted and adjusted models showed that an IPWC between 1 kg/m² and <3 kg/m² was significantly linked with s-GDM in the f-ND subgroup (Table 4). Model 2 further indicated a significant association between an IPWC of 1 kg/m² to <3 kg/m² and s-GDM in the f-YMA subgroup (Table 4). Conversely, no significant associations were observed between any IPWC categories and s-GDM in the subgroups of IPI ⩾ 36 months, f-AMA, f-GDM, f-OB, or f-UW (Table 4). An IPWC < -1 kg/m² also showed no significant association with s-GDM across any subgroup (P >0.05). In the f-GDM subgroup, no significant difference in s-GDM incidence was found between women with an IPWC of 1 kg/m² to <3 kg/m² and those with a stable IPWC (Supplementary Figure 1A). However, in the f-ND subgroup, women with an IPWC of 1 kg/m² to <3 kg/m² had a lower incidence of s-GDM compared to those with a stable IPWC (Supplementary Figure 1B). Furthermore, no significant interactions were observed across the various IPWC categories when analyzed with the four stratification factors ($P > 0.05$, Supplementary Table 2).

DISCUSSION

This single-center study conducted in China reveals a significant association between IPWC value and the risk of developing GDM during a second pregnancy, particularly when IPWC is ⩾3 kg/m² . Stratified analysis confirmed this association for participants with an IPI of 36 months or less, maternal age under 35, no previous GDM, and normal weight in their first pregnancy. In non-diabetic women, even an IPWC category of 1 kg/m² to <3 kg/m² is significantly associated with increased risk of GDM in the second pregnancy. Conversely, we did not observe this association in those with an IPI of 36 months or more, maternal age of 35 or older, previous GDM, or those who were overweight, obese, or underweight during their first pregnancy. Additionally, no significant correlation was found between IPWC less than -1kg/m² and the decreased risk of the GDM in the second pregnancy. This study provides valuable guidance for women aiming to prevent GDM in their second pregnancy by setting weight management goals.

The study identified a significant positive effect of IPWC⩾3 kg/m² on GDM in the second pregnancy across two different models, underscoring the reliability of this finding. Over the past decade, several studies conducted in different countries have suggested a potential link between interpregnancy weight change (IPWC) and the risk of s-GDM[17,16]. Whiteman et al.'s study identified a significant association between changes in BMI classification, particularly from normal to overweight or obese, and the risk of s-GDM[28]. Participants who experienced an increase in BMI had higher odds of developing s-GDM compared to those whose BMI remained unchanged[29]. In addition， the magnitude of the change in BMI was also thought to be associated with s-GDM risk. Earlier investigations suggested that an IPWC 3 kg/m² or more increased the likelihood of developing s-GDM, when compared to the stable IPWC category (±1kg/m²) [11]. Subsequent research by Bogaerts et al[9]. and Knight-Agarwal et al[30]. also confirmed this finding, which is consistent with the results in our study.

For IPWC of 1 kg/m² to <3 kg/m², its significant association with s-GDM was found only in Model 2 but not in Model 1, suggesting that the association between this category of IPWC and s-GDM needs to be further confirmed in the unstratified population. However, stratified analyses suggested that in the f-ND subgroup, both Model 1 and Model 2 revealed a significant association between IPWC 1 kg/m² to <3 kg/m² and s-GDM, and this consistent result was not seen in any other subgroup. Since there were cases of f-GDM in all subgroups except the f-ND subgroup, an

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

effect of f-GDM cannot be ruled out, which may help explain this difference. Women with a history of GDM have a high risk of recurrence in their next pregnancy[31]. Our study suggested that such women had a risk of GDM recurrence of more than 45% even if they maintained a stable IPWC (Supplementary Figure 1), which completely masked the effect of IPWC 1 kg/m² to <3 kg/m². The large influence of GDM history may make it difficult to achieve the goal of reducing GDM risk in the second pregnancy by controlling IPWC in this population.

Being overweight or obese prior to pregnancy is a significant risk factor for GDM[8]. Insulin resistance plays a crucial role in the development of GDM among individuals who are overweight[32]. Furthermore, excessive gestational weight gain (GWG) is closely linked to the occurrence of GDM[7,8].To mitigate the risk of GDM and macrosomia, the Institute of Medicine (IOM) suggests adopting appropriate GWG guidelines for singleton pregnancies based on pre-pregnancy weights[33]. Moreover, substantial weight gain before pregnancy has also been found to be associated with GDM[34]. Some observational studies[12,13, 35, 36] and two systematic reviews[16,37] have suggested that even IPWC categories ⩾1kg/m² is linked to a higher risk of GDM in the second pregnancy. Variations in the association between IPWC categories and s-GDM across studies may stem from differences in population criteria[36], diverse diagnostic standards for GDM[12,13, 35, 36], differing definitions of IPWC[35], or distinct confounding factors considered in relation to GDM[35, 13, 36]. It is essential to note that the outcomes of these studies may differ among various study groups. Our study, conducted within the Chinese population, enhances the findings of previous research largely centered on populations in developed countries. Furthermore, our results indicate that the risk of GDM in subsequent pregnancies increases by approximately 11% for each unit increase in IPWC value, aligning with the findings by Lyne Lynes et al. (OR=1.08, 95%CI: 1.05-1.10) [12]. Therefore, we suggest that controlling IPWC to less than 3 kg/m² may be effective in reducing the risk of GDM in the next pregnancy in Chinese population.

Unlike the overall study results, the results of stratified analysis suggested that the impact of IPWC on s-GDM varied in different subgroups. Even with the same IPWC categories, the risk of s-GDM differs based on IPI, maternal age, GDM status, or BMI in the first pregnancy. Stratified analysis revealed that IPWC categories ⩾3kg/m² had a more significant impact on the risk of s-GDM in participants with a shorter IPI compared to those with a longer IPI. Compared to an interval of 24 to 35 months, an interval ⩾36 months was associated with a higher risk of weight gain from the first to the second pregnancy[38]. Previous studies have also shown that women with GDM tend to gain weight faster before pregnancy compared to non-GDM women[39]. Therefore, it would be more reasonable to investigate the association between weight change and s-GDM within a narrower range of IPI[9]. Tano et al. 's study suggested that annual BMI gain was associated with the risk of GDM during the subsequent pregnancy[40]. These studies imply that the risk of s-GDM is not only associated with increased BMI units but also with the rate at which BMI increases by three units or more. The effect of IPI on s-GDM risk diminishes after 36 months between pregnancies.

In the stratified analysis by maternal age, our study identified a significant association between an IPWC of ⩾ 3 kg/m² and an increased risk of s-GDM in women under 35, but not in older women. For those with advanced maternal age, the incidence of GDM in their first pregnancy significantly rose, with GDM in a previous pregnancy being the most significant risk factor for s-GDM (OR:9.884), potentially masking the effect of IPWC. A study conducted in China found that women over the age of 30 had a higher risk of GDM compared to women aged

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

25 to 29 years old [41]. Additionally, the risk of GDM in Asian women was more strongly correlated with age starting at 25 years old, compared to Europid women[42]. Regrettably, no other stratified studies based on maternal age were identified in the existing literature. This finding has important implications in establishing weight control goals based on age. To further validate this hypothesis, further research with a larger sample size is necessary.

Similarly, stratified analysis based on BMI during the first pregnancy revealed that the association between IPWC and s-GDM was significant only in normal-weight women, with no significant link found in those who were overweight or obese. This contrasts with the findings of McBain et al. [6] and Ku et al. [36], who reported a significant relationship between IPWC and s-GDM across all BMI subgroups, with the larger IPWC category showing increased s-GDM risk particularly in the lower BMI subgroup. However, McBain et al. [6] used the interval -2 kg/m² < IPWC < 2 kg/m² as a reference and defined overweight or obesity as BMI⩾25 kg/m² , while Ku et al. [36] used a BMI cutoff of 23 kg/m² , potentially contributing to the differences in results. Given that overweight or obese women in our study had a higher risk of f-GDM (24.77%), we hypothesized that the absence of a significant association between IPWC and s-GDM among these women might stem from the influence of GDM during the first pregnancy. Although we did not find an interaction between IPWC and BMI categories, the possibility of an interaction involving IPWC, BMI category, and GDM status in the first pregnancy remains open for larger sample investigation. One study that stratified analyses by BMI and GDM status in the first pregnancy found that for overweight or obese women with GDM in their first pregnancy, the risk of GDM in a subsequent pregnancy was markedly higher if IPWC was ⩾4 units [43]. Conversely, without GDM in their first pregnancy, an IPWC >1 unit heightened their GDM risk in the second pregnancy[43]. Collectively, these findings imply that IPWC has a more pronounced impact on s-GDM risk in normal-weight women compared to those overweight or obese. The lack of an effect of IPWC on s-GDM in women who were underweight during their first pregnancy may be attributed to the necessity for greater weight gain to achieve a normal weight [44], thus not elevating s-GDM risk.

Our study did not find evidence to support the protective effect of IPWC <-1 kg/m² on s-GDM, which is consistent with the findings of other studies[12, 13, 30, 36]. We hypothesize that women with decreased IPWC might possess intrinsic risk factors for GDM, possibly related to their efforts in weight control, thereby not significantly reducing GDM risk in subsequent pregnancies. Three systematic analyses also yielded consistent results[14, 15, 17]. However, Martinez-Hortelano et al.'s stratified analyses suggest a decline in initial pre-pregnancy weight significantly reduced the risk of s-GDM in women with a BMI greater than 25kg/m² during their first pregnancy. This effect was not observed in women with a BMI less than 25kg/m² [37]. Conversely, a systematic analysis by Kirkegaard et al. found the opposite association: in women with a BMI less than 25 kg/m², a decrease in BMI was significantly associated with increased s-GDM risk[45]. Interestingly, Black et al.'s study found that for underweight or normal weight women with GDM in their first pregnancy, a decrease in BMI significantly increased the risk of GDM in a second pregnancy by 31% compared to maintaining a stable BMI [43]. These studies reveal ongoing uncertainty regarding the association between weight loss and GDM risk in different participant populations.

Certainly, this study has several limitations. Firstly, it is a retrospective, single-center study, with all data collected from historical databases. Some confounding factors, such as diet, family

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

history of diabetes, and gestational weight gain during the first pregnancy, were not included in the analysis, potentially impacting the results. Secondly, the sample size for certain subgroups, such as those who are overweight or obese and those with GDM in their first pregnancy with a BMI increase of three units or more, is relatively small, reducing statistical power. Thirdly, excluding women without BMI information may have introduced selection bias.

CONCLUSION

Our study in China revealed a clear correlation between the risk of GDM in the second pregnancy and the IPWC, specifically when the IPWC is $\geqslant 3$ kg/m^2. This relationship is particularly pronounced in women with an IPI shorter than 36 months, who are under 35 years old, have no history of GDM, or maintained a normal weight during their first pregnancy. For women without GDM in their first pregnancy, even an IPWC between 1 kg/m² and <3 kg/m² correlates with increased GDM risk in their second pregnancy. Conversely, we did not observe an association between GDM risk in the second pregnancy and an IPWC of < -1 kg/m². Further research with larger sample sizes is needed to confirm these findings, especially focusing on women who are overweight, obese, underweight, or had GDM during their first pregnancy.

Acknowledgments The authors thank all the participants in this study

Contributors SZ designed the study, supervised the work, reviewed and edited the manuscript. AY, YW, YL and JY collected the clinical data. SZ, AY, YW, YL and CX researched the data, performed the statistical analysis and wrote the manuscript. All authors have read and approved the final manuscript. SZ is the guarantor.

Funding This study was granted by the Shenzhen Science and Technology Innovation Program (JCYJ20210324110206017), the research project of Peking University Shenzhen Hospital (LCYJ2021010), Sanming Project of Medicine in Shenzhen (No.SZSM202011016) and Shenzhen High-level Hospital Construction Fund (YBH2019-260).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study protocol was approved by the Medical Ethics Committee of Peking University Shenzhen Hospital (#2023-103).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

References

1. Gao C, Sun X, Lu L, Liu F, Yuan J. Prevalence of gestational diabetes mellitus in mainland China: A systematic review and meta-analysis. *J Diabetes Investig*. 2019;10(1):154-162. doi:10.1111/jdi.12854
2. Goldstein RF, Abell SK, Ranasinha S, et al. Gestational weight gain across continents and ethnicity: systematic review and meta-analysis of maternal and infant outcomes in more than one million women. *BMC Med*. 2018;16(1):153. doi:10.1186/s12916-018-1128-1

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

3. Yamamoto JM, Kellett JE, Balsells M, et al. Gestational Diabetes Mellitus and Diet: A Systematic Review and Meta-analysis of Randomized Controlled Trials Examining the Impact of Modified Dietary Interventions on Maternal Glucose Control and Neonatal Birth Weight. *Diabetes Care*. 2018;41(7):1346-1361. doi:10.2337/dc18-0102
4. Zhang Y, Xiao CM, Zhang Y, et al. Factors Associated with Gestational Diabetes Mellitus: A Meta-Analysis. *J Diabetes Res*. 2021;2021. doi:10.1155/2021/6692695
5. Wu L, Cui L, Tam WH, Ma RCW, Wang CC. Genetic variants associated with gestational diabetes mellitus: a meta-analysis and subgroup analysis. *Sci Rep*. 2016;6:30539. doi:10.1038/srep30539
6. McBain RD, Dekker GA, Clifton VL, Mol BW, Grzeskowiak LE. Impact of inter-pregnancy BMI change on perinatal outcomes: a retrospective cohort study. *Eur J Obstet Gynecol Reprod Biol*. 2016;205:98-104. doi:10.1016/j.ejogrb.2016.07.487
7. Peng Y, Han N, Su T, et al. Gestational weight gain and the risk of gestational diabetes mellitus: A latent class trajectory analysis using birth cohort data. *Diabetes Res Clin Pract*. 2021;182:109130. doi:10.1016/j.diabres.2021.109130
8. Sun Y, Shen Z, Zhan Y, et al. Effects of pre-pregnancy body mass index and gestational weight gain on maternal and infant complications. *BMC Pregnancy Childbirth*. 2020;20(1):390. doi:10.1186/s12884-020-03071-y
9. Bogaerts A, Van Den Bergh BRH, Ameye L, et al. Interpregnancy weight change and risk for adverse perinatal outcome. In: *Obstetrics and Gynecology*. Vol 122. ; 2013:999-1009. doi:10.1097/AOG.0b013e3182a7f63e
10. Ehrlich SF, Hedderson MM, Feng J, Davenport ER, Gunderson EP, Ferrara A. Change in body mass index between pregnancies and the risk of gestational diabetes in a second pregnancy. *Obstet Gynecol*. 2011;117(6):1323-1330. doi:10.1097/AOG.0b013e31821aa358
11. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. *Lancet (London, England)*. 2006;368(9542):1164-1170. doi:10.1016/S0140-6736(06)69473-7
12. Lynes C, McLain AC, Yeung EH, Albert P, Liu J, Boghossian NS. Interpregnancy weight change and adverse maternal outcomes: a retrospective cohort study. *Ann Epidemiol*. 2017;27(10):632-637.e5. doi:10.1016/j.annepidem.2017.09.008
13. Sorbye LM, Skjaerven R, Klungsoyr K, Morken NH. Gestational diabetes mellitus and interpregnancy weight change: A population-based cohort study. *PLoS Med*. 2017;14(8):1-19. doi:10.1371/journal.pmed.1002367
14. Teulings NEWD, Masconi KL, Ozanne SE, Aiken CE, Wood AM. Effect of interpregnancy weight change on perinatal outcomes: Systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2019;19(1). doi:10.1186/s12884-019-2566-2
15. Timmermans YEG, van de Kant KDG, Oosterman EO, et al. The impact of interpregnancy weight change on perinatal outcomes in women and their children: A systematic review and meta-analysis. *Obes Rev*. 2020;21(3). doi:10.1111/obr.12974
16. Nagpal TS, Souza SCS, Moffat M, et al. Does prepregnancy weight change have an effect on subsequent pregnancy health outcomes? A systematic review and meta-analysis. *Obes Rev*. 2022;23(1). doi:10.1111/obr.13324
17. Oteng-Ntim E, Mononen S, Sawicki O, Seed PT, Bick D, Poston L. Interpregnancy weight change and adverse pregnancy outcomes: a systematic review and meta-analysis. *BMJ Open*.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

2018;8(6):e018778. doi:10.1136/bmjopen-2017-018778

18. International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy. *Diabetes Care*. 2010;33(3):676-682. doi:10.2337/dc09-1848

19. Yang Y, He R, Zhang N, Li L. Second-Child Fertility Intentions among Urban Women in China: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2023;20(4):3744. doi:10.3390/ijerph20043744

20. Zhu H, Zhao Z, Xu J, et al. The prevalence of gestational diabetes mellitus before and after the implementation of the universal two-child policy in China. *Front Endocrinol (Lausanne)*. 2022;13. doi:10.3389/fendo.2022.960877

21. Wastnedge EAN, Fretwell J, Johns EC, Denison FC, Reynolds RM. First and second pregnancy outcomes in women with class III obesity: An observational cohort study. *Obes Res Clin Pract*. 2021;15(4):357-361. doi:10.1016/j.orcp.2021.05.004

22. Liu J, Song G, Meng T, Zhao G, Guo S. Weight retention at six weeks postpartum and the risk of gestational diabetes mellitus in a second pregnancy. *BMC Pregnancy Childbirth*. 2019;19(1). doi:10.1186/s12884-019-2423-3

23. Ku CW, Cheng TS, Ku CO, et al. Distribution and association of interpregnancy weight change with subsequent pregnancy outcomes in Asian women. *Sci Rep*. 2023;13(1). doi:10.1038/s41598-023-31954-5

24. Chen K, Shen Z, Gu W, et al. Prevalence of obesity and associated complications in China: A cross-sectional, real-world study in 15.8 million adults. *Diabetes, Obes Metab*. 2023;25(11):3390-3399. doi:10.1111/dom.15238

25. Sparić R, Stojković M, Plešinac J, Pecorella G, Malvasi A, Tinelli A. Advanced maternal age (AMA) and pregnancy: a feasible but problematic event. *Arch Gynecol Obstet*. 2024;310(3):1365-1376. doi:10.1007/s00404-024-07678-w

26. He Y, Ma RCW, David Mcintyre H, et al. Comparing IADPSG and NICE Diagnostic Criteria for GDM in Predicting Adverse Pregnancy Outcomes. *Diabetes Care*. 2022;45(9):2046-2054. doi:10.2337/dc22-0579

27. Chou JS, Packer CH, Mittleman MA, Valent AM. Association of interpregnancy interval and gestational diabetes mellitus. *J Matern Fetal Neonatal Med*. 2022;35(26):10545-10550. doi:10.1080/14767058.2022.2134770

28. Whiteman VE, Aliyu MH, August EM, et al. Changes in prepregnancy body mass index between pregnancies and risk of gestational and type 2 diabetes. *Arch Gynecol Obstet*. 2011;284(1):235-240. doi:10.1007/s00404-011-1917-7

29. Bender W, Hirshberg A, Levine LD. Interpregnancy Body Mass Index Changes: Distribution and Impact on Adverse Pregnancy Outcomes in the Subsequent Pregnancy. *Am J Perinatol*. 2019;36(5):517-521. doi:10.1055/s-0038-1670634

30. Knight-Agarwal CR, Williams LT, Davis D, et al. Association of BMI and interpregnancy BMI change with birth outcomes in an Australian obstetric population: A retrospective cohort study. *BMJ Open*. 2016;6(5). doi:10.1136/bmjopen-2015-010667

31. Egan AM, Enninga EAL, Alrahmani L, Weaver AL, Sarras MP, Ruano R. Recurrent Gestational Diabetes Mellitus: A Narrative Review and Single-Center Experience. *J Clin Med*. 2021;10(4):569. doi:10.3390/jcm10040569

32. Zhu Y, Hedderson MM, Quesenberry CP, Feng J, Ferrara A. Central Obesity Increases the

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Risk of Gestational Diabetes Partially Through Increasing Insulin Resistance. *Obesity (Silver Spring)*. 2019;27(1):152-160. doi:10.1002/oby.22339

33. *Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines. Weight Gain During Pregnancy: Reexamining the Guidelines. Rasmussen KM, Yaktine AL, Editors. Washington (DC): National Academies Press (U.*

34. Diouf I, Charles MA, Thiebaugeorges O, et al. Maternal weight change before pregnancy in relation to birthweight and risks of adverse pregnancy outcomes. *Eur J Epidemiol*. 2011;26(10):789-796. doi:10.1007/s10654-011-9599-9

35. Ehrlich SF, Hedderson MM, Feng J, Davenport ER, Gunderson EP, Ferrara A. Change in body mass index between pregnancies and the risk of gestational diabetes in a second pregnancy. *Obstet Gynecol*. 2011;117(6):1323-1330. doi:10.1097/AOG.0b013e31821aa358

36. Ku CW, Cheng TS, Ku CO, et al. Distribution and association of interpregnancy weight change with subsequent pregnancy outcomes in Asian women. *Sci Rep*. 2023;13(1):1-10. doi:10.1038/s41598-023-31954-5

37. Martínez-Hortelano JA, Cavero-Redondo I, Álvarez-Bueno C, Díez-Fernández A, Hernández-Luengo M, Martínez-Vizcaíno V. Interpregnancy Weight Change and Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Obesity (Silver Spring)*. 2021;29(2):454-464. doi:10.1002/oby.23083

38. Ziauddeen N, Roderick PJ, Macklon NS, Alwan NA. The duration of the interpregnancy interval in multiparous women and maternal weight gain between pregnancies: findings from a UK population-based cohort. *Sci Rep*. 2019;9(1):9175. doi:10.1038/s41598-019-45595-0

39. Thompson M Lou, Ananth C V, Jaddoe VW V, Miller RS, Williams MA. The association of maternal adult weight trajectory with preeclampsia and gestational diabetes mellitus. *Paediatr Perinat Epidemiol*. 2014;28(4):287-296. doi:10.1111/ppe.12128

40. Tano S, Kotani T, Ushida T, et al. Annual Body Mass Index Gain and Risk of Gestational Diabetes Mellitus in a Subsequent Pregnancy. *Front Endocrinol (Lausanne)*. 2022;13(March):1-10. doi:10.3389/fendo.2022.815390

41. Cao J, Xu W, Liu Y, et al. Trends in maternal age and the relationship between advanced age and adverse pregnancy outcomes: a population-based register study in Wuhan, China, 2010–2017. *Public Health*. 2022;206:8-14. doi:10.1016/j.puhe.2022.02.015

42. Li Y, Ren X, He L, Li J, Zhang S, Chen W. Maternal age and the risk of gestational diabetes mellitus: A systematic review and meta-analysis of over 120 million participants. *Diabetes Res Clin Pract*. 2020;162:108044. doi:10.1016/j.diabres.2020.108044

43. Black KI, Schneuer F, Gordon A, Ross GP, Mackie A, Nassar N. Estimating the impact of change in pre-pregnancy body mass index on development of Gestational Diabetes Mellitus: An Australian population-based cohort. *Women and Birth*. 2022;35(6):563-569. doi:10.1016/j.wombi.2021.12.007

44. Lyu J, Sun Y, Ji Y, et al. Optimal Gestational Weight Gain for Women with Gestational Diabetes Mellitus — China, 2011–2021. *China CDC Wkly*. 2023;5(9):189-193. doi:10.46234/ccdcw2023.034

45. Kirkegaard H, Bliddal M, Støvring H, et al. Maternal weight change from prepregnancy to 18 months postpartum and subsequent risk of hypertension and cardiovascular disease in Danish women: A cohort study. *PLoS Med*. 2021;18(4):e1003486. doi:10.1371/journal.pmed.1003486

For peer review only

Enseignement Superieur (ABES) .

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Figure 1 Flow chart showing inclusion and exclusion in this study *BMI: body mass index; IPWC: interpregnancy weight change.*

Figure 2 The frequencies of the IPWC categories and their distributions in different subgroups *The frequencies of four IPWC categories showed right-skewed (A); Subgroup of IPI ⩾36 months owned a larger proportion of IPWC 1 to < 3 kg/m²and a smaller proportion of stable IPWC (B);The proportion of four IPWC categories did not differ between f-GDM and f-ND group (C); Overweight or obese women owned a larger proportion of IPWC < -1kg/m²and a smaller proportion of IPWC of 1 kg/m² to < 3 kg/m² (D).IPWC: interpregnancy weight change; IPI: inerpregnancy interval; GDM: gestational diabetes mellitus; UW: underweight; NW: normal weight; OB: overweight or obese; f-: in the first pregnancy.*

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Table 1 Comparison of the IPWC and other risk factors between s-GDM and s-ND groups

risk factors	s-GDM group (n=303)	s-ND group (n=2069)	difference of mean or OR (95% CI) for s-GDM
continuous variables			
IPWC [kg/m^2 (interquartile range)]	0.970(-0.150-2.110)	0.680(-0.250-1.730)	**0.221(0.000-0.442)**
f-MA (years)	29.29±3.53	28.10±3.28	**1.184(0.785-1.583)**
f-BMI (kg/m^2)	21.33±3.02	20.36±2.55	**0.963(0.604-1.321)**
s-BMI (kg/m^2)	22.30±3.31	21.12±2.81	**1.184(0.791-1.576)**
IPI [months (interquartile range)]	36.16(26.07-48.53)	30.95(22.25-46.25)	**4.398(2.579-6.218)**
categorical variables			
IPWC categories			
< -1 kg/m^2	32(10.56)	253(12.23)	0.848(0.574-1.251)*
-1 kg/m^2 to < 1 kg/m^2	124(40.92)	984(47.56)	**0.764(0.598-0.976)** *
1 kg/m^2 to < 3 kg/m^2	105(34.65)	645(31.17)	1.171(0.908-1.510) *
≥ 3 kg/m^2	42(13.86)	187(9.04)	**1.620(1.131-2.319)** *
Han nationality [n (%)]	289(95.38)	1966(95.02)	1.081(0.611-1.916)
f-ART [n (%)]	20(6.60)	100(4.83)	1.392(0.847-2.285)
f-GDM [n (%)]	126(41.58)	139(6.72)	**9.884(7.425-13.157)**
f-HDCP [n (%)]	20(6.60)	61(2.95)	**2.326(1.383-3.914)**
f-hypothyroidism [n (%)]	14(4.62)	118(5.70)	0.801(0.454-1.413)
f-hyperthyroidism [n (%)]	2(0.66)	16(0.77)	0.853(0.195-3.726)
f-APS [n (%)]	0(0.00)	4(0.19)	-
f-SLE [n (%)]	0(0.00)	12(0.58)	-
f-PPH [n (%)]	8(2.64)	34(1.64)	1.623(0.744-3.540)
f-PCOS [n (%)]	2(0.66)	4(0.19)	3.43(0.626-18.808)
f-CS [n (%)]	125(41.25)	610(29.48)	**1.68(1.311-2.151)**
f-PTB [n (%)]	23(7.59)	108(5.22)	1.492(0.935-2.380)
f-macrosomia [n (%)]	18(5.94)	81(3.91)	1.55(0.916-2.622)
f-male newborn [n (%)]	148(48.84)	1033(49.93)	0.958(0.752-1.219)
f-AMA	24(7.92)	62(3.00)	**2.785(1.710-4.534)**
f-UW	49(16.17)	485(23.44)	**0.701(0.505-0.974)**
f-OB	50(16.50)	168(8.12)	**2.066(1.458-2.926)**
IPI ⩾36 months	152(50.17)	795(38.42)	**1.613(1.266-2.055)**

f: in previous pregnancy; s: in the second pregnancy; * the corresponding IPWC category was analyzed as binary variable; MA: maternal age; BMI: body mass index; IPWC: interpregnancy weight change; IPI: interpregnancy interval; ART: assisted reproductive technology; GDM: gestational diabetes mellitus; HDCP: hypertensive disorder complicating pregnancy; APS: antiphospholipid syndrome; SLE: systemic lupus erythematosus; PPH: postpartum hemorrhage; PCOS: polycystic ovary syndrome; CS: cesarean section; PTB: preterm birth; OR: odds ratio; CI: confidence interval.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

Table 2 The effect of IPWC on the GDM in the second pregnancy in unadjusted and adjusted models

	unadjusted OR (95% CI)	adjusted OR (95% CI) in Model 1*	adjusted OR (95% CI) in Model 2 #
IPWC value	1.067(1.000-1.139)	**1.105(1.029-1.186)**	**1.111(1.038-1.190)**
IPWC categories			
< -1 kg/m^2	1.004(0.664-1.516)	0.837(0.528-1.327)	0.799(0.508-1.259)
-1 kg/m^2 to < 1 kg/m^2	reference	reference	reference
1 kg/m^2 to < 3 kg/m^2	1.292(0.978-1.706)	1.350(0.996-1.832)	**1.364(1.009-1.842)**
≥ 3 kg/m^2	**1.782(1.215-2.615)**	**1.797(1.173-2.754)**	**1.821(1.197-2.772)**

IPWC: interpregnancy weight change; GDM: gestational diabetes mellitus. * adjusted by IPI, f-BMI, f-AMA, f-GDM, f-HDCP, f-macrosomia, f-PTB, and f-CS; # adjusted by f-BMI and f-GDM.

Table 3 The effect of IPWC value on the GDM in the second pregnancy in stratified subgroups

Population included	unadjusted model		Model 1*		Model 2 #	
	OR (95% CI)	P for interaction	adjusted OR (95% CI)	P for interaction	adjusted OR (95% CI)	P for interaction
IPI≥36 months (n=947)	1.069(0.970-1.180)	0.846	1.091(0.984-1.210)	0.885	1.097(0.990-1.215)	0.968
IPI < 36 months (n=1425)	1.055(0.966-1.154)		**1.118(1.014-1.232)**		**1.116(1.015-1.227)**	
f-AMA (n=86)	1.034(0.786-1.360)	0.761	1.075(0.754-1.533)	0.862	1.052(0.776-1.427)	0.978
f-YMA (n=2286)	**1.08(1.010-1.156)**		**1.11(1.032-1.194)**		**1.12(1.043-1.202)**	
f-GDM (n=265)	1.034(0.786-1.360)	0.693	1.094(0.967-1.239)	0.607	1.099(0.974-1.241)	0.758
f-ND (n=2107)	**1.096(1.008-1.191)**		**1.116(1.024-1.216)**		**1.117(1.028-1.214)**	
f-OB (n=218)	1.079(0.943-1.235)	0.926	1.093(0.941-1.271)	0.982	1.082(0.938-1.248)	0.927
f-NW (n=1620)	**1.096(1.011-1.188)**		**1.119(1.024-1.222)**		**1.126(1.033-1.228)**	
f-UW (n=534)	1.126(0.952-1.332)		1.084(0.882-1.331)		1.105(0.924-1.322)	

p: in previous pregnancy; IPWC: interpregnancy weight change; IPI: interpregnancy interval; AMA: advanced maternal age; YMA: young maternal age; GDM: gestational diabetes mellitus; ND: non-diabetic status; OB: overweight or obese; NW: normal weight; UW: underweight. * adjusted by IPI, f-BMI, f-AMA, f-GDM, f-HDCP, f-macrosomia, f-PTB, and f-CS; # adjusted by f-BMI and f-GDM.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Table 4 The effect of IPWC categories on the GDM in second pregnancy in stratified subgroups

Population included	OR (95% CI)			
	< -1 kg/m^2	-1 kg/m^2 to < 1 kg/m^2	1 kg/m^2 to < 3 kg/m^2	≥ 3 kg/m^2
unadjusted model				
IPI⩾36 months (n=947)	1.151(0.630-2.103)	reference	1.470(0.990-2.184)	1.618(0.908-2.883)
IPI < 36 months (n=1425)	0.893(0.505-1.581)	reference	1.052(0.704-1.572)	**1.886(1.129-3.151)**
f-AMA (n=86)	0.972(0.263-3.595)	reference	1.591(0.483-5.237)	1.458(0.236-8.997)
f-YMA (n=2286)	0.984(0.636-1.525)	reference	1.323(0.992-1.766)	**1.852(1.249-2.747)**
f-GDM (n=265)	0.764(0.355-1.644)	reference	1.039(0.591-1.827)	1.718(0.760-3.882)
f-ND (n=2107)	1.036(0.604-1.774)	reference	**1.463(1.028-2.082)**	**1.831(1.119-2.993)**
f-OB (n=218)	0.882(0.395-1.967)	reference	1.200(0.529-2.724)	1.964(0.646-5.966)
f-NW (n=1620)	0.885(0.529-1.481)	reference	1.294(0.923-1.815)	**1.777(1.119-2.820)**
f-UW (n=534)	-	reference	1.554(0.823-2.936)	1.849(0.739-4.624)
Model 1*				
IPI⩾36 months (n=947)	0.851(0.429-1.685)	reference	1.446(0.943-2.216)	1.417(0.751-2.675)
IPI < 36 months (n=1425)	0.872(0.464-1.639)	reference	1.272(0.816-1.984)	**2.298(1.287-4.104)**
f-AMA (n=86)	1.298(0.265-6.365)	reference	1.710(0.418-6.987)	3.230(0.394-26.466)
f-YMA (n=2286)	0.838(0.515-1.363)	reference	1.362(0.994-1.866)	**1.813(1.170-2.808)**
f-GDM (n=265)	0.643(0.287-1.444)	reference	1.058(0.589-1.900)	1.770(0.759-4.129)
f-ND (n=2107)	0.965(0.552-1.686)	reference	**1.522(1.063-2.179)**	**1.900(1.151-3.135)**
f-OB (n=218)	0.860(0.342-2.160)	reference	1.218(0.464-3.196)	2.050(0.549-7.659)
f-NW (n=1620)	0.834(0.475-1.464)	reference	1.319(0.914-1.904)	**1.907(1.148-3.170)**
f-UW (n=534)	-	reference	1.415(0.702-2.854)	1.394(0.480-4.048)
Model 2#				
IPI⩾36 months (n=947)	0.782(0.398-1.537)	reference	1.396(0.915-2.131)	1.422(0.757-2.669)
IPI < 36 months (n=1425)	0.799(0.428-1.494)	reference	1.208(0.780-1.871)	**2.210(1.251-3.904)**
f-AMA (n=86)	0.808(0.193-3.389)	reference	1.390(0.382-5.055)	1.790(0.255-12.584)
f-YMA (n=2286)	0.798(0.494-1.289)	reference	**1.395(1.022-1.905)**	**1.854(1.204-2.857)**
f-GDM (n=265)	0.623(0.282-1.376)	reference	1.096(0.618-1.943)	1.722(0.752-3.941)
f-ND (n=2107)	0.901(0.520-1.559)	reference	**1.486(1.044-2.117)**	**1.872(1.143-3.065)**
f-OB (n=218)	0.992(0.411-2.394)	reference	1.367(0.553-3.380)	1.815(0.521-6.327)
f-NW (n=1620)	0.760(0.435-1.330)	reference	1.296(0.901-1.864)	**1.936(1.174-3.193)**
f-UW (n=534)	-	reference	1.575(0.804-3.084)	1.472(0.549-3.947)

f: in previous pregnancy; IPWC: interpregnancy weight change; IPI: interpregnancy interval; AMA: advanced maternal age; YMA: young maternal age; GDM: gestational diabetes mellitus; ND: non-diabetic status; OB:

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

overweight or obese; NW: normal weight; UW: underweight. * adjusted by IPI, f-BMI, f-AMA, f-GDM, f-HDCP, f-macrosomia, f-PTB, and f-CS; # adjusted by f-BMI and f-GDM.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

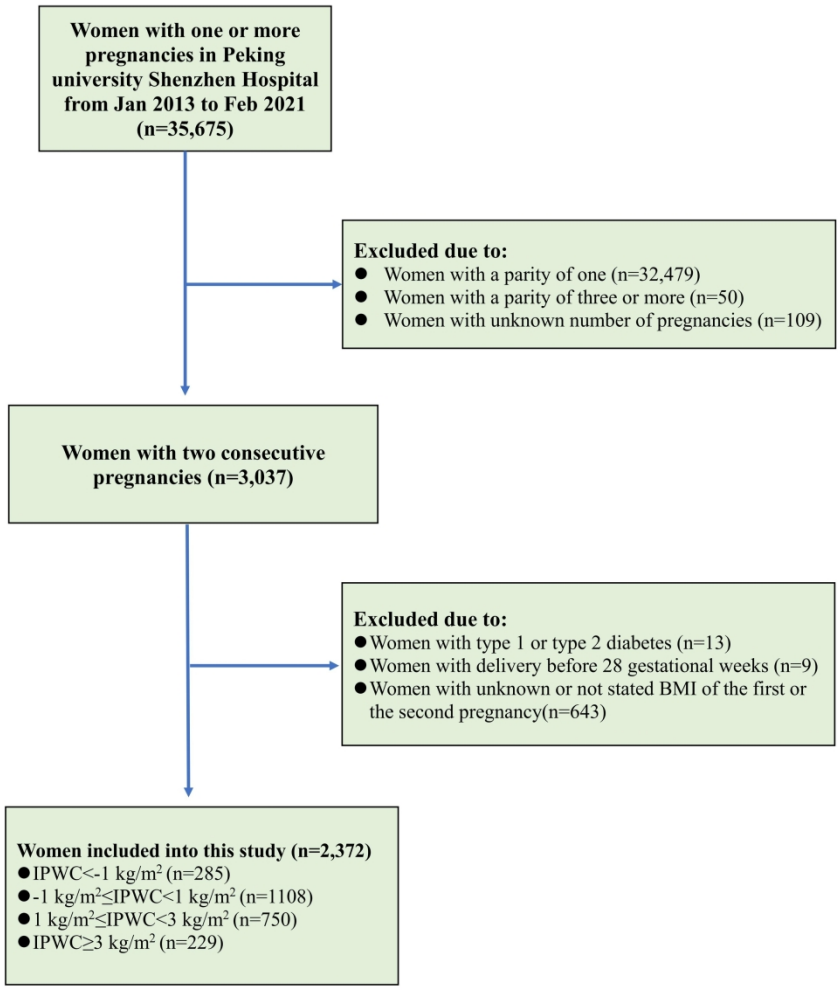


Figure 1 Flow chart showing inclusion and exclusion in this study BMI: body mass index; IPWC: interpregnancy weight change.

209x296mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

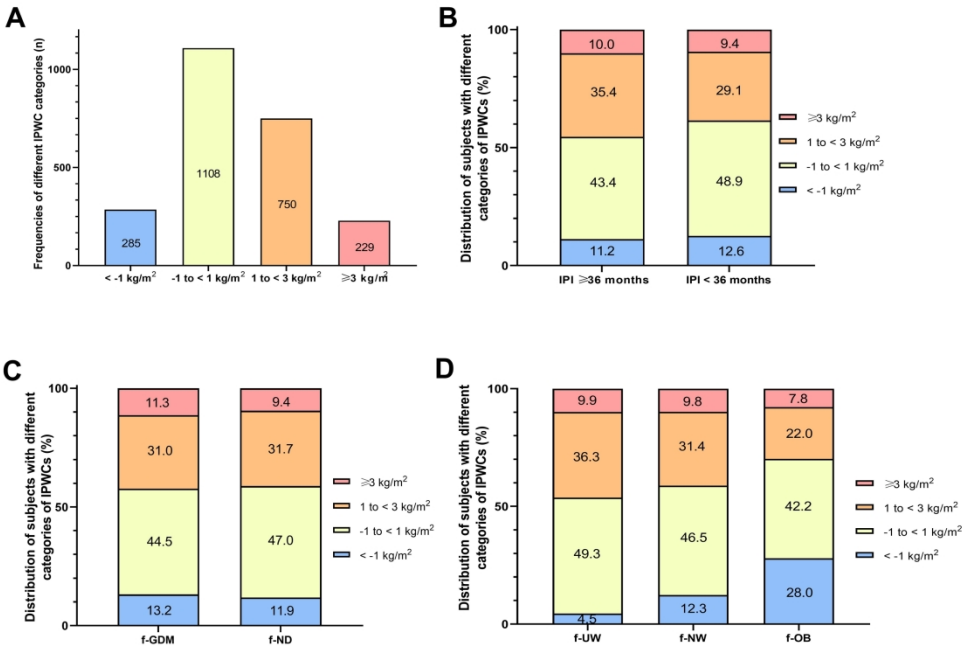


Figure 2 The frequencies of the IPWC categories and their distributions in different subgroups The frequencies of four IPWC categories showed right-skewed (A); Subgroup of IPI ≥36 months owned a larger proportion of IPWC 1 to < 3 kg/m²and a smaller proportion of stable IPWC (B);The proportion of four IPWC categories did not differ between f-GDM and f-ND group (C); Overweight or obese women owned a larger proportion of IPWC < -1kg/m²and a smaller proportion of IPWC of 1 kg/m2 to < 3 kg/m2 (D).IPWC: interpregnancy weight change; IPI: inerpregnancy interval; GDM: gestational diabetes mellitus; UW: underweight; NW: normal weight; OB: overweight or obese; f-: in the first pregnancy.

251x172mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2024-084282 on 23 January 2025. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Supplementary Table 1 Collinearity analysis of the independent variables

variables	tolerance	VIF
IPWC value	0.957	1.044
IPI	0.139	7.219
f-MA	0.021	47.898
s-MA	0.018	55.443
f-BMI	0.928	1.077
s-BMI*	0.000	-

f: in the first pregnancy; s: in the second pregnancy; BMI: body mass index; IPWC: interpregnancy weight change; IPI: interpregnancy interval; VIF: variance inflation factor; MA: advanced maternal age; * this variable was excluded during the analysis;

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

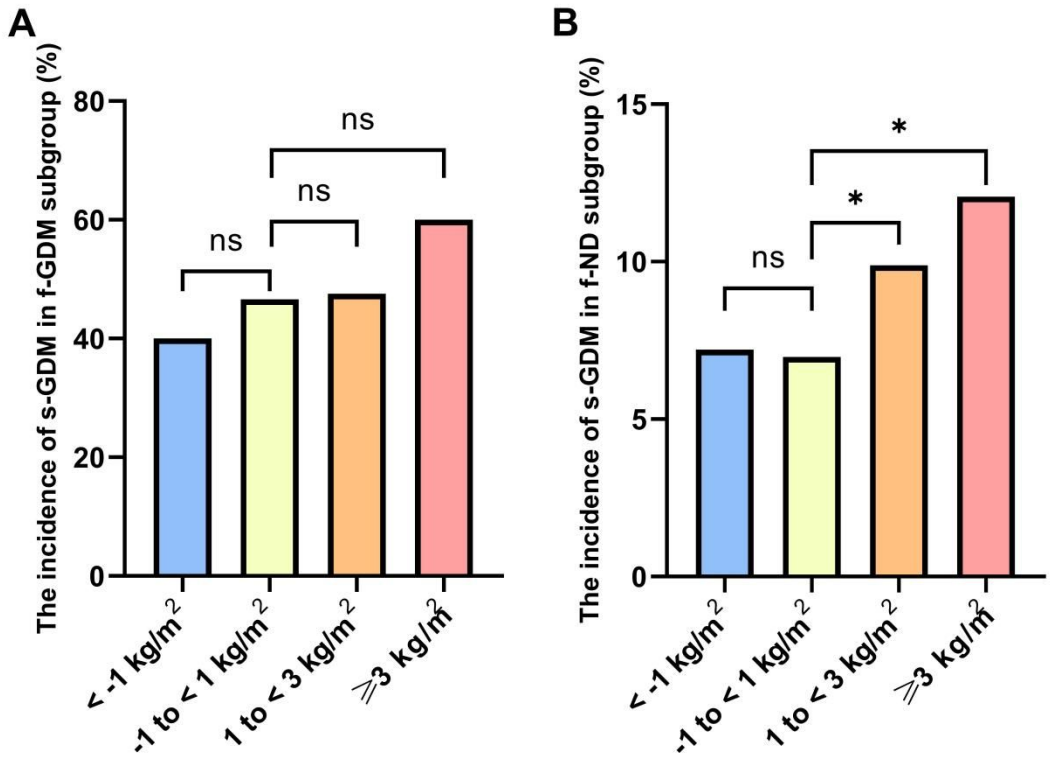
Supplementary Table 2 The interaction effect of IPWC categories with stratified factors for the s-GDM risk

variables	adjusted OR*	95% CI*
IPWC categories interacted with IPI categories		
IPWC < -1 kg/m^2 interacted with IPI ≥36 months	0.756	0.396-1.442
-1 kg/m^2≤IPWC <1 kg/m^2 interacted with IPI ≥36 months	reference	reference
1 kg/m^2≤IPWC <3 kg/m^2 interacted with IPI ≥36 months	1.393	0.951-2.042
IPWC ≥3 kg/m^2 interacted with IPI ≥36 months	1.322	0.715-2.446
IPWC categories interacted with f-AMA		
IPWC < -1 kg/m^2 interacted with s-AMA	0.707	0.156-3.211
-1 kg/m^2≤IPWC <1 kg/m^2 interacted with f-AMA	reference	reference
1 kg/m^2≤IPWC <3 kg/m^2 interacted with f-AMA	1.540	0.399-5.943
IPWC ≥3 kg/m^2 interacted with f-AMA	1.603	0.205-12.518
IPWC categories interacted with f-GDM		
IPWC < -1 kg/m^2 interacted with f-GDM	0.618	0.278-1.375
-1 kg/m^2≤IPWC <1 kg/m^2 interacted with f-GDM	reference	reference
1 kg/m^2≤IPWC <3 kg/m^2 interacted with f-GDM	0.984	0.550-1.761
IPWC ≥3 kg/m^2 interacted with f-GDM	1.602	0.691-3.711
IPWC categories interacted with the BMI categories of the first trimester*		
IPWC < -1 kg/m^2 interacted with f-UW	-	-
-1 kg/m^2≤IPWC <1 kg/m^2 interacted with f-UW	reference	reference
1 kg/m^2≤IPWC <3 kg/m^2 interacted with f-UW	1.144	0.668-1.961
IPWC ≥3 kg/m^2 interacted with f-UW	1.145	0.458-2.858
IPWC < -1kg/m^2 interacted with f-OB	0.794	0.358-1.762
-1 kg/m^2≤IPWC <1 kg/m^2 interacted with f-OB	reference	reference
1 kg/m^2≤IPWC <3 kg/m^2 interacted with f-OB	1.213	0.530-2.776
IPWC ≥3 kg/m^2 interacted with f-OB	1.820	0.533-6.212

f: in the first pregnancy; IPWC: interpregnancy weight change; IPI: interpregnancy interval; AMA: advanced maternal age; GDM: gestational diabetes mellitus; OB: overweight or obese; UW: underweight; *adjusted by IPI, f-BMI, f-AMA, f-GDM, f-HDCP, f-macrosomia, f-PTB, and f-CS.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .



Supplementary figure 1 The incidences of s-GDM in in f-GDM subgroup (A) and f-DN subgroup (B) *s-GDM: gestational diabetes mellitus in the second pregnancy; f-GDM: gestational diabetes mellitus in the first pregnancy; f-DN: non-diabetic status in the first pregnancy. ns: no significance; * P <0.05.*

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .