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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
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Keywords:	Diabetes in pregnancy < DIABETES & ENDOCRINOLOGY, OBSTETRICS, Weight Gain, Maternal medicine < OBSTETRICS, Risk Factors





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

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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/m²), 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 \geq 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 \geq 3 units was only showed in participants with IPI \leq 36 months(aOR: 2.165, 95%CI: 1.214-3.860), BMI \geq 21kg/m²(aOR: 2.256, 95%CI: 1.135-4.483), or maternal age \geq 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

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

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].

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/m²) and was divided into seven categories: $\leq -3kg/m^2$, $-3 kg/m^2$ 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 $\geq 3 kg/m^2$. 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 (\geq 24.0 kg/m²). 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 \geq 5.1 mmol/L at 0 hours, and/or \geq 10.0 mmol/L at 1 hour, and/or \geq 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

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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 \pm 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,

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 $\ge 3 \text{ kg/m}^2$ 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/m² 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 \leq 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/m², 23kg/m², 22kg/m², and 21kg/m². Only when the BMI cut-off value was equal to 21kg/m² 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/m², 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/m², 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

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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 $\geq 3 \text{kg/m}^2$ 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 prepregnancy 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].

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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 \geq 36 months was associated with a higher risk of weight gain from the first to the second pregnancy^[30]. Previous studies have also shown

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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 \geq 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/m², 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/m²). In a study conducted by McBain et al., they suggested that an IPWC ≥ 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 ± 1 unit as a reference. In their study, an IPWC ≥ 1 unit significantly increased the risk of GDM in the subgroup with a BMI greater than 23 kg/m², while an IPWC \geq 3 units increased the risk of GDM in the subgroup with a BMI less than 23 kg/m² ^[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 \geq 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 ≥ 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,

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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/m² during their first pregnancy. This effect was not observed in women with a BMI less than 25kg/m² ^[28]. 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 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

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University Shenzhen Hospital (#2023-103).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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Figure 1 Flow chart showing inclusion and exclusion in this study

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

Risk factors	Total (n=2372)	GDM group (n=303)	non-GDM group (n=2069)	$t/Z/\chi^2$	Р
maternal age (years, $x\pm s$) ^a	28.27±3.35	29.29±3.53	28.10 ± 3.28	5.815	0.00
Han nationality	2255(95.07)	289(95.38)	1966(95.02)	0.072	0.78
BMI (kg/m ²) ^a	20.49±2.64	21.33±3.02	20.36±2.55	5.279	0.00
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	0.00
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	0.00
ART [n (%)] ^a	120(5.06)	20(6.6)	100(4.8)	1.719	0.19
GDM [n (%)] ^a	265(11.17)	126(41.6)	139(6.7)	323.750	0.00
HDCP [n (%)] ^a	81(3.41)	20(6.6)	61(2.9)	2.847	0.09
hypothyroidism [n (%)]ª	132(5.56)	14(4.6)	118(5.7)	0.590	0.44
hyperthyroidism [n (%)] ^a	18(0.76)	2(0.7)	16(0.8)	0.045	0.83
APS [n (%)] ^a	4(0.17)	0(0)	4(0.2)	0.587	0.44
SLE [n (%)] ^a	12(0.51)	0(0)	12(0.6)	1.766	0.18
PPH [n (%)] ^a	42(1.77)	8(2.6)	34(1.6)	1.510	0.21
PCOS [n (%)] ^a	6(0.25)	2(0.7)	4(0.2)	2.282	0.13
CS [n (%)] ^a	735(30.99)	125(41.3)	610(29.5)	17.125	0.00
PTB [n (%)] ^a	131(5.52)	23(7.6)	108(5.2)	2.847	0.09
macrosomia [n (%)] ^a	99(4.17)	18(5.9)	81(3.9)	2.712	0.10
male newborn [n (%)] ^a	1181(49.79)	148(48.8)	1033(49.9)	0.124	0.72

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^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.

variables	regression coefficient	standard error	Wald value	P	OR	05%CI for O
$\frac{1}{1} Variables}$	0 113	0.463	0.059	0.808	1 119	0 452-2 771
$-3 \text{ kg/m}^2 < \text{IPWC} < -2 \text{ kg/m}^2$	-0.056	0.453	0.015	0.902	0.946	0.389-2.299
$-2 \text{ kg/m}^2 \leq IPWC < -1 \text{ kg/m}^2$	-0.124	0.290	0.183	0.669	0.883	0.500-1.560
-1 kg/m ² \leq IPWC <1 kg/m ²	reference	reference	reference	reference	reference	reference
$1 \text{ kg/m}^2 \leq \text{IPWC} \leq 2 \text{ kg/m}^2$	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 $\geq 3 \text{ kg/m}^2$	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	6.982-12.71
HDCP ^a	0.539	0.310	3.028	0.082	1.714	0.934-3.143
macrosomiaª	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.

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ppp(<-3.1gam)					Adjusted C	OR and 95%CI		B
Implementation 0.8330(0192.41) 0.700(0212.727) 1.0450(04992.119) 1.000 1.430(0492.2236) 0.830(04441.759) 2.1460(1214.258) IPS Manuality 1.320(0192.41) 1.220(0301.248) 0.340(0305.159) 1.000 1.320(0302.236) 0.830(0441.759) 2.140(0371.236) IDM = Thank - 0.990(0301.225) 0.740(0301.236) 1.000 1.320(0802.248) 1.340(0852.270) 1.340(085		IPWC < -3 kg/m ²	-3 kg/m ² \leq IPWC <- 2 kg/m ²	$-2 \text{ kg/m}^2 \leq \text{IPWC} < -1 \text{ Kg/m}^2$	Den _1 kg/m²≤IPWC <1 kg/m²	$\frac{1 \text{ kg/m}^2 \leq \text{IPWC} < 2}{\text{kg/m}^2}$	$\frac{2 \text{ kg/m}^2 \leq IPWC <3}{\text{kg/m}^2}$	Pa IPWC≥3 kg/m ²
(1)************************************	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)
All \$12 hyp (\$13 hyp) (\$13 hyp) 	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)
and s-1 sing (-6-33) (-6-33) (-6-33) (-6-33) (-6-33) (-6-3) (-	BMI $\leq 21 \text{ kg/m}^2$	-	-	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)
	(n=1334) BMI >21 kg/m ² (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)
Section 2012 2760(58)-9249 10990(254-425) 1070(684-618) 1.00 1590(8151304) 0.550(185-184) 2.80(1064-6157) 1070(684-618) 1.00 1590(8151304) 0.550(185-184) 2.80(1064-6157) 1070(684-618) 1.00 1590(8151304) 0.550(185-184) 2.80(1064-6157) 1.00 1.00 1590(8151304) 0.550(185-184) 2.80(1064-6157) 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.0	maternal age≤30	0.665(0.176-	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)
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/m ² .	maternal age>30	2.313)	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)
^a n this subgroup, there were no cases of GDM in the second pregnancy if the IPWC was less than -2 kg/m ² .	years (II=302)	Table 3 Adju	sted OR values	of IPWC for the	GDM risk i	in the second pr	egnancy in strat	tified
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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, Al training, and similar technologies.

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## **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 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 Xu, Chang; Intelligent Hospital Research Academy, 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
<b>Primary Subject Heading</b> :	Obstetrics and gynaecology
Secondary Subject Heading:	Obstetrics and gynaecology
Keywords:	Diabetes in pregnancy < DIABETES & ENDOCRINOLOGY, OBSTETRICS, Weight Gain, Maternal medicine < OBSTETRICS, Risk Factors

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9	3	population: a retrospective cohort study
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12	5	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}
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32	20	
34	21	Abstract
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36	22	<b>Objectives</b> This study aimed to investigate the impact of interpregnancy weight changes (IPWC)
3/ 12	23	on the risk of gestational diabetes mellitus (GDM) in the second pregnancy.
89	24	Design A retrospective cohort study.
0	25	Setting Data were collected in Peking University Shenzhen Hospital from 2013 Jan to 2021 Feb.
1	26	Participants Women who had two consecutive singleton deliveries after 28 gestational weeks
12	27	(N=2372).
רי 14	28	Outcomes The risk of GDM in the second pregnancy.
15	29	Methods: IPWC was divided into seven categories by units BMI (kg/m ² ), with the range of -1
6	30	kg/m ² to 1 kg/m ² being used as the reference range. Adjusted odds ratios (aORs) with 95% CIs
7	31	were obtained by multivariable logistic regression models to evaluate the association between the
ю 19	32	IPWC and GDM. Analyses were stratified by interpregnancy interval (IPI), maternal age. GDM.
50	33	BMI in the first pregnancy.
51	34	<b>Results:</b> IPWC is significantly positively associated with the GDM during the second pregnancy
2	25	(aOR 1 443 [95% CI 1 026-2 031] for BMI gain of 1 to 2 kg/m ² aOR 1 818 [05% CI 1 104 2 767]
53 54	35	for BMI gain of $\geq 3 \text{ kg/m}^2$ : a QR 1.111 [05% CI 1.028 1.100] for par units increase of continuous
<b>7</b>	20	IDW(C) No significant link was found between intermediate DML determed $CDM$ is
55	3/	1  FWC. No significant link was found between interpregnancy BMI decrease and GDM risk
55 56	20	$(D \cap O \cap C)$ Structure density manual defined density $C \to C$ is the UDWC $> 2$ is the
55 56 57	38	( <i>P</i> >0.05). Stratified analysis revealed that the significant association between IPWC $\geq$ 3 units and
55 56 57 58 59	38 39	( <i>P</i> >0.05). Stratified analysis revealed that the significant association between IPWC $\geq$ 3 units and GDM risk was only showed in participants with IPI less than 36 months (aOR 2.217, 95%CI

(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

► 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.

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 weight², diet³, maternal age⁴, exercise, and genetics⁵. 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 GDM⁸.

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 review¹⁷ 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  $\geq$ 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 2010¹⁸, 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 child¹⁹. A higher proportion of advanced maternal age (>30 years) and multiparity have increased the risk of GDM²⁰. 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.

97 MATERIALS ADN METHODS

#### 98 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.

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- 108 Patient and Public Involvement statement
  - 109 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/m²), was categorized into seven groups:  $\leq -3$  kg/m², -3 kg/m² 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/m² to <2 kg/m², 2 kg/m² to < 3 kg/m², and  $\ge$ 3 kg/m². Participants were classified into four BMI categories: underweight (<18.5 kg/m²), normal weight (18.5 kg/m² to <24.0 kg/m²), and overweight or obese ( $\geq$ 24.0 kg/m²). 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

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

124 The primary outcome of the study was the presence of GDM in the second pregnancy. 125 Throughout the entire study period, GDM was diagnosed using the IADPSG criteria²⁵, which 126 involved a 75-gram oral glucose tolerance test. According to these criteria, a diagnosis of GDM 127 was made if the serum blood glucose levels were  $\geq 5.1$  mmol/L at 0 hour, and/or  $\geq 10.0$  mmol/L 128 at 1 hour, and/or  $\geq 8.5$  mmol/L at 2 hour, between 24-28 weeks of gestation.

#### 129 Data collection

130 The data for this study were obtained from the delivery records within the hospital 131 information system. The collected variables include: IPI, maternal age, BMI, parity, year of 132 delivery, delivery mode, occupation, medical payment method, ethnicity, marital status, sex of 133 newborn, birth weight, BMI of the first trimester during the first and second pregnancies, and the 134 occurrence of GDM, thyroid disease, hypertensive disorder complicating pregnancy (HDCP), and 135 preterm birth.

#### 136 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  $\ge$  36 months) ²⁶, maternal age ( $\ge$  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.

#### 160 Statistical method

161The data analysis was performed using SPSS 24.0 statistical software (IBM, Armonk, NY,162USA). Categorical variables were presented as n (%) and compared using the Chi-square test.

#### 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  $28.25 \pm 3.33$  years, with a mean BMI of  $20.48 \pm 2.64$  kg/m² and an average gestational age at delivery of  $38.82 \pm 1.53$  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  $31.15 \pm 3.57$  years, with a mean BMI of 21.27 $\pm$  2.90 kg/m² and a mean gestational age at delivery of 38.54  $\pm$  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  $\leq$  -3 kg/m², ranging from -3  $kg/m^2$  to  $<-2 kg/m^2$ , from  $-2 kg/m^2$  to  $<-1 kg/m^2$ , from  $-1 kg/m^2$  to  $<1 kg/m^2$ , from  $1 kg/m^2$  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  $\leq$  -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  $\leq -1$  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 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  $\ge 3 \text{ kg/m}^2$  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

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 ( $\chi$ 2=4.474, P=0.034), while the proportion of IPWC  $\geq$  3 units was significantly higher ( $\chi$ 2=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 The effect of the IPWC categories and continuous IPWC value on the GDM in BMI in the first trimester, continuous interpregnancy interval (IPI), maternal age, gestational diabetes mellitus (GDM), hypertensive disorders in pregnancy (HDCP), macrosomia, preterm

(Table 1).

the second pregnancy

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  $\geq 3$  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  $\ge$  36 months, maternal age  $\ge$  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  $\ge 3$  kg/m² (Table 4). However, in subgroups such as those with an IPI  $\geq$  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

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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  $\ge 3 \text{ kg/m}^2$  on GDM in the second pregnancy across two different models, underscoring the reliability of this finding. However, for the category 1 kg/m²  $\le$  IPWC<2 kg/m², 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/m²  $\le$  IPWC<2 kg/m² 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 GDM⁸. Insulin resistance plays a crucial role in the development of GDM among individuals who are overweight²⁷. 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 prepregnancy weights²⁸. Moreover, substantial weight gain before pregnancy has also been found to be associated with GDM²⁹.

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 GDM³⁰. Participants who experienced an increase in BMI had higher odds of developing GDM compared to those whose BMI remained unchanged³¹. 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  $(\pm 1 \text{ kg/m}^2)^{-11}$ . Subsequent research by Bogaerts et al⁹. and Knight-Agarwal et al³². 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 criteria³⁴, diverse diagnostic standards for GDM^{12,13, 33, 34}, differing definitions of IPWC³³, or distinct confounding factors considered in relation to GDM^{33, 13, 34}. 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 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  $\geq$  36 months was associated with a higher risk of weight gain from the first to the second pregnancy³⁶. Previous studies have also shown that women with GDM tend to gain weight faster before pregnancy compared to non-GDM women³⁷. Therefore, it would be more reasonable to investigate the association between weight change and GDM within a narrower range of IPI9. Tano et al. 's study suggested that annual BMI gain was associated with the risk of GDM during the subsequent pregnancy³⁸. 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  $\ge$  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 women⁴⁰. 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/m² < IPWC < 2 kg/m² as a reference and defined overweight or obesity as BMI $\ge$  25 kg/m², while Ku et al. ³⁴ used a BMI cutoff of 23 kg/m², 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

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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  $\geq$ 4 units ⁴¹. Conversely, without GDM in their first pregnancy, an IPWC >1 unit heightened their GDM risk in the second pregnancy⁴¹. 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  $-1 \text{ kg/m}^2$  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/m² during their first pregnancy. This effect was not observed in women with a BMI less than 25kg/m² ³⁵. Conversely, a systematic analysis by Kirkegaard et al. found the opposite association: in women with a BMI less than  $25 \text{ kg/m}^2$ , a decrease in BMI was significantly associated with increased GDM risk⁴³. 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 BMI⁴¹. These studies reveal ongoing uncertainty regarding the association between weight loss and GDM risk in different participant populations.

362 Certainly, this study has several limitations. Firstly, it is a retrospective, single-center study, 363 with all data collected from historical databases. Some confounding factors, such as diet, family 364 history of diabetes, and gestational weight gain during the first pregnancy, were not included in 365 the analysis, potentially impacting the results. Secondly, the sample size for certain subgroups, 366 such as those who are overweight or obese and those with GDM in their first pregnancy with a 367 BMI increase of three units or more, is relatively small, reducing statistical power. Thirdly, 368 excluding women without BMI information may have introduced selection bias. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

#### 369 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.

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3 4	378	Acknowledgments The authors thank all the participants in this study
5	379	<b>Contributors</b> SZ designed the study, supervised the work, reviewed and edited the manuscript.
6 7	380	AY, YW, YL and JY collected the clinical data. AY, YW, YL and CX researched the data,
8	381	performed the statistical analysis and wrote the manuscript. SZ is the guarantor. All authors have
9	382	read and approved the final manuscript.
10	202	
11	383	Funding This study was granted by the Shenzhen Science and Technology Innovation Program
12	384	(JCYJ20210324110206017), the research project of Peking University Shenzhen Hospital
14	385	(LCYJ2021010), Sanming Project of Medicine in Shenzhen (No.SZSM202011016) and Shenzhen
15 16	386	High-level Hospital Construction Fund (YBH2019-260).
17 18	387	Competing interests None declared.
19	388	Patient consent for publication Not required.
20	389	<b>Ethics approval</b> The study protocol was approved by the Medical Ethics Committee of Peking
22 23	390	University Shenzhen Hospital (#2023-103).
24 25	391	Provenance and peer review Not commissioned; externally peer reviewed.
26 27	392	Data availability statement Data are available upon reasonable request.
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30 31	526	
32	527	Figure 1 Flow chart showing inclusion and exclusion in this study <i>BMI: body mass index; IPWC:</i>
33	528	interpregnancy weight change.
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546		Table 1 The pr	oportion of variou	s IPWCs in differ	ent BMI and GD	M categorizes on 20		
		IPWC < $-3$ kg/m ² [n(%)]	-3 kg/m ² ≤IPWC <-2 kg/m ² [n(%)]	$-2 \text{ kg/m}^2 \le \text{IPWC}$ <-1 kg/m ² [n(%)]	-1 kg/m ² ≤IPWC <1 kg/m ² [n(%)]	1 kg/m²≤∰PWa <2 kg/m²∰2	$2 \text{ kg/m}^2 \leq \text{IPWC}$ $< 3 \text{ kg/m}^2 [n(\%)]$	IPWC $\geq 3 \text{ kg/n}$ [n(%)]
	BMI categories in the first pregnancy				<b></b>	ary 202 seigne s relate		
	overweight or obese (n=218)	25(11.47)	15(6.88)	21(9.63)	92(42.20)	^{29(13.30)} m 25.	19(8.72)	17(7.80)
	normal weight (n=1620)	23(1.42)	39(2.41)	141(8.70)	750(46.30)	316(1945) an Cupper	192(11.85)	159(9.81)
	underweight (n=534)	0(0.00)	3(0.56)	21(3.93)	263(49.25)	141(26 data	53(9.93)	53(9.93)
	GDM in the first pregnancy					a mini		
	yes (n=265)	10(3.77)	8(3.02)	17(6.42)	118(44.53)	51(19 <b>)</b> <b>A</b>	31(11.70)	30(11.32)
	no (n=2107)	38(1.80)	49(2.33)	166(7.88)	987(46.84)		233(11.06)	199(9.44)
	GDM in the second pregnancy				9	ng, ar		
	yes (GDM group) (n=303)	8(2.64)	7(2.31)	17(5.61)	124(40.92)*	69(22 <b>4</b> 7) <b>icon</b>	36(11.88)	42(13.86)**
547	no (non-GDM group) (n=2069)	40(1.93)	50(2.42)	166(8.02)	981(47.41)*		228(11.02)	187(9.04)**
547 548 559 550 551 552 553	n we. incipregnancy weight change, Dwn. ood	iy mass meex, OD	vi. gestational diabete	s memus. 1 < 0.03	, 1 <0.01	une 7, 2025 at Agence Biblic schnologies.		
-		For peer rev	iew only - http://br	njopen.bmj.com/	site/about/guidel	ographique de l ines.xhtml		

Risk factors	Total (n=2372)		GDM group (n=303)	non-GDM gr (n=2069)	oup Differ e of m or O	enc ean 95% CI R
maternal age (years, $x\pm s$ )*	28.27	/±3.35	29.29±3.53	28.10±3.2	8 1.18	0.785-1.583
Han nationality[n (%)]*	2255(	95.07)	289(95.38)	1966(95.02	2) 1.08	0.611-1.916
BMI $(kg/m^2)^*$	20.49	±2.64	21.33±3.02	20.36±2.5	5 0.96	0.604-1.321
(interquartile range)]	0.725(-0.2	240-1.770)	0.970(-0.150-2.110)	0.680(-0.250-1	.730) 0.22	1 0.000-0.442
BMI in the second pregnancy (kg/m ² )	21.27	±2.90	22.30±3.31	21.12±2.8	1 1.18	4 0.791-1.576
IPI [months (interquartile range)	] 31.68(22.	.50-43.56)	36.16(26.07-48.53)	30.95(22.25-4	6.25) 4.39	2.579-6.218
ART [n (%)]*	120(	5.06)	20(6.60)	100(4.83)	1.39	0.847-2.285
$GDM [n (\%)]^*$	265(1	11.17)	126(41.58)	139(6.72)	9.88	4 7.425-13.157
HDCP [n (%)]*	81(3	3.41)	20(6.60)	61(2.95)	2.32	6 1.383-3.914
hypothyroidism [n (%)]*	132(	5.56)	14(4.62)	118(5.70)	0.80	0.454-1.413
hyperthyroidism [n (%)]*	18(0	).76)	2(0.66)	16(0.77)	0.85	0.195-3.726
APS [n (%)]*	4(0	.17)	0(0.00)	4(0.19)	-	-
SLE [n (%)]*	12(0	0.51)	0(0.00)	12(0.58)	-	-
PPH [n (%)]*	42(1	1.77)	8(2.64)	34(1.64)	1.62	3 0.744-3.540
PCOS [n (%)]*	6(0	.25)	2(0.66)	4(0.19)	3.43	0 0.626-18.808
CS [n (%)]*	735(3	30.99)	125(41.25)	610(29.48	) 1.68	0 1.311-2.151
PTB [n (%)]*	131(	5.52)	23(7.59)	108(5.22)	1.49	2 0.935-2.380
macrosomia [n (%)]*	99(4	4.17)	18(5.94)	81(3.91)	1.55	0 0.916-2.622
male newborn [n (%)]*	1181(-	49.79)	148(48.84)	1033(49.93	3) 0.95	8 0.752-1.219
male newborn [n (%)]* 555 *in the first pregr	nancy; BMI: boo	49.79) dy mass index; I	148(48.84) PWC: interpregnancy v	1033(49.93 weight change; IPI: into	3) 0.95 erpregnancy inte	8 0.752-1.219 rval;
male newborn [n (%)]* 555 * in the first pregr 556 ART: assisted r	nancy; BMI: boo reproductive tec	49.79) dy mass index; I chnology; GDN	148(48.84) PWC: interpregnancy v f: gestational diabetes	1033(49.93 weight change; IPI: into mellitus; HDCP: h	3) 0.95 erpregnancy inte ypertensive disc	8 0.752-1.219 rval;
male newborn [n (%)]* 555 * in the first pregr 556 ART: assisted r 557 complicating pre	nancy; BMI: boo reproductive tec	49.79) dy mass index; I chnology; GDN ntiphospholipid	148(48.84) PWC: interpregnancy v f: gestational diabetes syndrome: SLE: system	1033(49.93 weight change; IPI: into mellitus; HDCP: hypic lupus ervthematos	crpregnancy inte pertensive discus: PPH: postpa:	8 0.752-1.219 rval; order rtum
male newborn [n (%)]* 555 * in the first pregr 556 ART: assisted r 557 complicating pre 558 hemograps: PC	1181( nancy; BMI: boo reproductive tec gnancy; APS: a	49.79) dy mass index; I chnology; GDM ntiphospholipid	148(48.84) PWC: interpregnancy w f: gestational diabetes syndrome; SLE: system	1033(49.93 weight change; IPI: into mellitus; HDCP: hy nic lupus erythematos	b) 0.95 erpregnancy inte ypertensive disc us; PPH: postpa DP: Odds Patio	8 0.752-1.219 rval; order rtum
male newborn [n (%)]* 555 * in the first pregr 556 ART: assisted r 557 complicating pre 558 hemorrhage; PC	1181( nancy; BMI: boo reproductive tec regnancy; APS: a OS: polycystic	49.79) dy mass index; I chnology; GDN ntiphospholipid ovary syndrome	148(48.84) PWC: interpregnancy v f: gestational diabetes syndrome; SLE: system c; CS:cesarean section;	1033(49.93 weight change; IPI: into a mellitus; HDCP: hy nic lupus erythematos PTB: preterm birth; C	b) 0.95 erpregnancy inte ypertensive disc us; PPH: postpa DR: Odds Ratio	8 0.752-1.219 rval; order rtum ; CI:
male newborn [n (%)]*         555       * in the first pregr         556       ART: assisted r         557       complicating pre         558       hemorrhage; PCC         559       confidence interv	1181( nancy; BMI: boo reproductive tec gnancy; APS: a OS: polycystic val.	49.79) dy mass index; I chnology; GDN ntiphospholipid ovary syndrome	148(48.84) PWC: interpregnancy v f: gestational diabetes syndrome; SLE: system c; CS:cesarean section;	1033(49.93 weight change; IPI: into mellitus; HDCP: hy nic lupus erythematos PTB: preterm birth; (	erpregnancy inte ypertensive disc us; PPH: postpa DR: Odds Ratio	8 0.752-1.219 rval; order rtum ; CI:
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male newborn [n (%)]*555* in the first pregr556ART: assisted r557complicating pre558hemorrhage; PC559confidence interv560561562Table 3 The e563multivariable avariablesIPWC <-3 kg/m²	1181( nancy; BMI: boo reproductive teo gnancy; APS: a OS: polycystic val. ffect of IPWC analysis non-ac OR 1. 582 1. 108 0. 810 reference 1. 309	49.79) dy mass index; I chnology; GDM ntiphospholipid ovary syndrome C categories o djusted 95% CI 0.724–3.458 0.491–2.497 0.475–1.380 reference 0.954–1.795	148(48.84) PWC: interpregnancy w f: gestational diabetes syndrome; SLE: system c; CS:cesarean section; mod adjusted OR 0. 830 0. 831 0. 826 reference 1. 414	1033(49.93         weight change; IPI: into         a mellitus; HDCP: hy         mic lupus erythematos         PTB: preterm birth; O         second pregnancy i         del 1*         95% CI         0. 326-2. 114         0. 341-2. 023         0. 466-1. 463         reference         1. 001-1. 997	b) 0.95 erpregnancy interpregnancy interpregnancy interpregnancy interpresented by postparation of the second state of the se	8 0.752-1.219 rval; order rtum ; CI: and del 2 [#] 95% CI 0. 324-1.955 0. 346-2.004 0. 438-1.364 reference 1. 026-2. 031
male newborn [n (%)]*555* in the first pregr556ART: assisted r557complicating pre558hemorrhage; PCC559confidence interv560561562Table 3 The e563multivariable avariablesIPWC <-3 kg/m²	1181(         nancy; BMI: boo         reproductive tec         egnancy; APS: a         OS: polycystic         val.         ffect of IPWC         analysis         non-ac         OR         1. 582         1. 108         0. 810         reference         1. 309         1. 249	49.79) dy mass index; I chnology; GDN ntiphospholipid ovary syndrome C categories o djusted 95% CI 0.724-3.458 0.491-2.497 0.475-1.380 reference 0.954-1.795 0.839-1.860	148(48.84) PWC: interpregnancy w f: gestational diabetes syndrome; SLE: system c; CS:cesarean section; mode adjusted OR 0. 830 0. 831 0. 826 reference 1. 414 1. 231	1033(49.93         weight change; IPI: into         a mellitus; HDCP: hy         nic lupus erythematos         PTB: preterm birth; O         second pregnancy i         del 1*         95% CI         0. 326-2. 114         0. 326-2. 114         0. 341-2. 023         0. 466-1. 463         reference         1. 001-1. 997         0. 792-1. 912	b) 0.95 erpregnancy interpregnancy interpregnancy interpregnancy interpresentation of the second state of	8 0.752-1.219 rval; order rtum ; CI: and del 2 [#] 95% CI 0. 324-1.955 0. 346-2.004 0. 438-1.364 reference 1. 026-2.031 0. 793-1.880
male newborn [n (%)]*555* in the first pregr556ART: assisted r557complicating pre558hemorrhage; PCC559confidence interv560561562Table 3 The er563multivariable avariablesIPWC <-3 kg/m²	1181( nancy; BMI: boo reproductive teo gnancy; APS: a OS: polycystic o /al. ffect of IPWC analysis non-ac OR 1.582 1.108 0.810 reference 1.309 1.249 1.777	49.79) dy mass index; I chnology; GDM ntiphospholipid ovary syndrome C categories o djusted 95% CI 0. 724-3. 458 0. 491-2. 497 0. 475-1. 380 reference 0. 954-1. 795 0. 839-1. 860 <b>1. 211-2. 607</b>	148(48.84)         PWC: interpregnancy w         f: gestational diabetes         syndrome; SLE: system         e; CS:cesarean section;         mode         adjusted OR         0.830         0.831         0.826         reference         1.414         1.231         1.794	1033(49.93 veight change; IPI: inte is mellitus; HDCP: hy nic lupus erythematos: PTB: preterm birth; O second pregnancy i del 1* 95% CI 0. 326-2. 114 0. 341-2. 023 0. 466-1. 463 reference 1. 001-1. 997 0. 792-1. 912 1. 170-2. 749	a) 0.95 erpregnancy interpregnancy interpregnancy interpregnancy interpresentation (pertensive discuss; PPH: postpara DR: Odds Ration DR: Odds Ration (DR: Odd) (DR: Odd) (DR	8 0.752-1.219 rval; order rtum ; CI: and odel 2 [#] 95% CI 0. 324–1. 955 0. 346–2. 004 0. 438–1. 364 reference 1. 026–2. 031 0. 793–1. 880 1. 194–2. 767
male newborn [n (%)]*555* in the first pregr556ART: assisted r557complicating pre558hemorrhage; PCC559confidence interv560561562Table 3 The er563multivariable avariablesIPWC <-3 kg/m²	1181( nancy; BMI: boo reproductive teo gnancy; APS: a OS: polycystic /al. ffect of IPWC analysis non-ac OR 1.582 1.108 0.810 reference 1.309 1.249 1.777 II of the first trir	49.79) dy mass index; I chnology; GDM ntiphospholipid ovary syndrome C categories o djusted 95% CI 0.724-3.458 0.491-2.497 0.475-1.380 reference 0.954-1.795 0.839-1.860 1.211-2.607 nester, continuo	148(48.84) PWC: interpregnancy w f: gestational diabetes syndrome; SLE: system c; CS:cesarean section; mod adjusted OR 0.830 0.831 0.826 reference 1.414 1.231 1.794 us interpregnancy inter	1033(49.93 weight change; IPI: into a mellitus; HDCP: hy mic lupus erythematos PTB: preterm birth; O second pregnancy i del 1* 95% CI 0. 326-2. 114 0. 341-2. 023 0. 466-1. 463 reference 1. 001-1. 997 0. 792-1. 912 1. 170-2. 749 val (IPI), maternal age,	b) 0.95 erpregnancy inter ypertensive disc us; PPH: postpa DR: Odds Ration DR: Odds Ration adjusted OR 0. 796 0. 833 0. 772 reference 1. 443 1. 221 1. 818 GDM, hyperter	8 0.752-1.219 rval; order rtum ; CI: and odel 2 [#] 95% CI 0. 324-1.955 0. 346-2.004 0. 438-1.364 reference 1. 026-2.031 0. 793-1.880 1. 194-2.767 nsive
male newborn [n (%)]*555* in the first pregr556ART: assisted r557complicating pre558hemorrhage; PCC559confidence interv560561562Table 3 The e563multivariable avariablesIPWC <-3 kg/m²	1181(         nancy; BMI: boo         reproductive tec         egnancy; APS: a         OS: polycystic         val.         ffect of IPWC         analysis         non-ac         OR         1. 582         1. 108         0. 810         reference         1. 309         1. 249         1. 777         II of the first trir         cating pregnance	49.79) dy mass index; I chnology; GDN ntiphospholipid ovary syndrome C categories o djusted 95% CI 0. 724-3. 458 0. 491-2. 497 0. 475-1. 380 reference 0. 954-1. 795 0. 839-1. 860 1. 211-2. 607 mester, continuo cy (HDCP), ma	148(48.84)         PWC: interpregnancy w         f: gestational diabetes         syndrome; SLE: system         c; CS:cesarean section;         mode         adjusted OR         0.830         0.831         0.826         reference         1.414         1.231         1.794         us interpregnancy intermosomia, preterm del	1033(49.93         weight change; IPI: into         a mellitus; HDCP: hy         nic lupus erythematos         PTB: preterm birth; O         second pregnancy i         del 1*         95% CI         0. 326-2. 114         0. 326-2. 114         0. 341-2. 023         0. 466-1. 463         reference         1. 001-1. 997         0. 792-1. 912         1. 170-2. 749         val (IPI), maternal age;         livery, and cesarean of	b) 0.95 erpregnancy inter ypertensive disc us; PPH: postpa DR: Odds Ration Adjusted OR 0.796 0.833 0.772 reference 1.443 1.221 1.818 GDM, hyperter delivery in the	8 0.752-1.219 rval; order rtum ; CI: and odel 2 [#] 95% CI 0. 324-1.955 0. 346-2.004 0. 438-1.364 reference 1. 026-2.031 0. 793-1.880 1. 194-2.767 usive first
male newborn [n (%)]*555* in the first pregr556ART: assisted r557complicating pre558hemorrhage; PCC559confidence interv560561562Table 3 The er563multivariable avariablesIPWC <-3 kg/m²	1181(         nancy; BMI: boo         reproductive tec         gnancy; APS: a         OS: polycystic         val.         ffect of IPWC         analysis         non-ac         OR         1.582         1.108         0.810         reference         1.309         1.249         1.777         II of the first trir         cating pregnance         sted by BMI of	49.79) dy mass index; I chnology; GDM ntiphospholipid ovary syndrome C categories o djusted 95% CI 0.724-3.458 0.491-2.497 0.475-1.380 reference 0.954-1.795 0.839-1.860 1.211-2.607 mester, continuo cy (HDCP), ma	148(48.84)         PWC: interpregnancy w         f: gestational diabetes         syndrome; SLE: system         e; CS:cesarean section;         mode         adjusted OR         0.830         0.831         0.826         reference         1.414         1.231         1.794         us interpregnancy intermores         ucrosomia, preterm defined	1033(49.93         weight change; IPI: intervieweight change; IPI: intervieweight change; IPI: intervieweight change; IPI: preterm birth; O         second pregnancy i         mic lupus erythematos:         PTB: preterm birth; O         second pregnancy i         del 1*         95% CI         0. 326-2. 114         0. 326-2. 114         0. 341-2. 023         0. 466-1. 463         reference         1. 001-1. 997         0. 792-1. 912         1. 170-2. 749         val (IPI), maternal age,         toregnancy: IPWC: in	<ul> <li>0.95</li> <li>crpregnancy integration of the second sec</li></ul>	8 0.752-1.219 rval; order rtum ; CI: and odel 2 [#] 95% CI 0. 324-1. 955 0. 346-2. 004 0. 438-1. 364 reference 1. 026-2. 031 0. 793-1. 880 1. 194-2. 767 nsive first eight
male newborn $[n (\%)]^*$ 555* in the first pregr556ART: assisted r557complicating pre558hemorrhage; PCC559confidence interv560561562Table 3 The er563multivariable avariablesIPWC < -3 kg/m²	1181( nancy; BMI: boo reproductive teo gnancy; APS: a OS: polycystic /al. ffect of IPWC analysis non-ac OR 1.582 1.108 0.810 reference 1.309 1.249 1.777 II of the first trir cating pregnance isted by BMI of astational disher	49.79) dy mass index; I chnology; GDM ntiphospholipid ovary syndrome C categories o djusted 95% CI 0. 724–3. 458 0. 491–2. 497 0. 475–1. 380 reference 0. 954–1. 795 0. 839–1. 860 1. 211–2. 607 mester, continuo cy (HDCP), ma The first trimest tas mellitus: OP	148(48.84) PWC: interpregnancy w f: gestational diabetes syndrome; SLE: system c; CS:cesarean section; mod adjusted OR 0.830 0.831 0.826 reference 1.414 1.231 1.794 us interpregnancy inter- ucrosomia, preterm del er and GDM in the firs : Odds Patio: CL corf.	1033(49.93         weight change; IPI: into         a mellitus; HDCP: hy         mic lupus erythematos         PTB: preterm birth; O         second pregnancy i         del 1*         95% CI         0. 326-2.114         0. 326-2.114         0. 326-2.114         0. 341-2.023         0. 466-1.463         reference         1.001-1.997         0.792-1.912         1.170-2.749         val (IPI), maternal age,         livery, and cesarean of         t pregnancy; IPWC: in	b) 0.95 erpregnancy inter ypertensive disc us; PPH: postpa DR: Odds Ration Adjusted OR 0. 796 0. 833 0. 772 reference 1. 443 1. 221 1. 818 GDM, hyperter delivery in the terpregnancy wo	$\begin{array}{c} 8 & 0.752-1.219 \\ \hline 8 & 0.752-1.219 \\ \hline 7 val; \\ \hline 9 rval; \\ \hline order \\ rtum \\ ; CI: \\ \hline \\ and \\ \hline \\ \hline \\ 0.324-1.955 \\ \hline \\ 0.324-1.955 \\ \hline \\ 0.324-1.955 \\ \hline \\ 0.346-2.004 \\ \hline \\ 0.438-1.364 \\ \hline \\ reference \\ \hline \\ 1.026-2.031 \\ \hline \\ 0.793-1.880 \\ \hline \\ 1.194-2.767 \\ \hline \\ nsive \\ first \\ eight \\ \hline \end{array}$

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571		stratified sub	ogroups			
Population included	non	adjusted	moo	del 1*	mod	el 2 #
i opulation metaded	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	1.038-1.19
IPI $\geq$ 36 months (n=947)	1.069	0.970-1.180	1.091	0.984-1.210	1.097	0.990-1.21
IPI < 36 months (n=1425)	1.055	0.966-1.154	1.118	1.014-1.232	1.116	1.015-1.22
naternal age≥35 years old ^{\$} (n=86)	1.034	0.786-1.360	1.075	0.754-1.533	1.052	0.776-1.42
maternal age < 35 years ^{\$} (n=2286)	1.080	1.010-1.156	1.110	1.032-1.194	1.120	1.043-1.2
GDM ^{\$} (n=265)	1.034	0.786-1.360	1.094	0.967-1.239	1.099	0.974-1.24
without GDM ^{\$} (n=2107)	1.096	1.008-1.191	1.116	1.024-1.216	1.117	1.028-1.2
overweight or obese $(n=2.18)$	1.079	0.943-1.235	1.093	0.941-1.271	1.082	0.938-1.24
normal weight $(n=1620)$	1.096	1.011-1.188	1.119	1.024-1.222	1.126	1.033-1.2
underweight $(n=534)$	1.126	0.952-1.332	1.084	0.882-1.331	1.105	0.924-1.3
572 * adjusted by continuous	IPWC value	MI of the first trime	ster continuous i	nterpregnancy inter	val (IPI) maternal	
572 aga CDM hypertensive	disordor com	lighting programa	(UDCD) magrage	amia protorm daliu	var (111), material	
575 age, ODW, hypertensive		plicating pregnancy	(HDCF), macros	onna, preterni den	very, and cesarean	
5/4 delivery in the first preg	mancy; # adjust	ed by BMI of the fu	st trimester and	GDM in the first p	regnancy; [•] in the	
575 first pregnancy.						
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adjusted OR (95% C1)           adjusted OR (95% C1)           adjusted OR (95% C1)           adjusted OR (95% C1)           by the problem of the pr	C	501		stratified analysis			
Population included         IPWC < .3 kg/m ² -3 kg/m ² SPWC <2 kg/m ² -2 kg/m ² SPWC <2 kg/m ² -1 kg/m ²						adjı	usted OR (95% CI)
Model I*       IP[≈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 (0.842-2.2)         IP1 < 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 (0.906~2.4)         maternal age ≥35 years       1.907 (0.958~62.300)       -       3.559 (0.549 ⁻ )       reference       1.396 (0.975~1.9)         (n=2286)       0.679 (0.167~2.680)       0.597 (0.133~2.675)       0.646 (0.218~1.389)       reference       1.996 (0.975~1.9)         Without GDM ⁴ (n=2107)       1.008 (0.288~3.523)       0.987 (0.333~2.925)       0.925 (0.473~1.807)       reference       1.537 (1.627~2.9)         werweight or obese [#] 0.649 (0.179~2.366)       2.125 (0.517~8.744)       0.595 (0.138~2.559)       reference       1.330 (0.870~2.0)         underweight [#] (n=1620)       1.257 (0.320~4.931)       0.397 (0.108~1.459)       0.930 (0.255~1.30)       reference       1.330 (0.870~2.0)         underweight [#] (n=1620)       1.257 (0.320~4.931)       0.397 (0.108~1.459)       0.930 (0.491~1.763)       reference       1.330 (0.823~2.13         Model 2*       IP1 < 36 months (n=947)       1.107 (0.321~3.816)       1.009 (0.291-3.490)       0.620 (0.255~1.500)       reference       1.442 (0.883~2.33)         reference <th>Рор</th> <th>ulation included</th> <th>IPWC $&lt; -3 \text{ kg/m}^2$</th> <th>-3 kg/m²$\leq$IPWC &lt;-2 kg/m²</th> <th>$\begin{array}{c} -2 \text{ kg/m}^2 \leq \text{IPWC} &lt; -1 \\ \text{kg/m}^2 \end{array}$</th> <th>-1 kg/m²≤IPWC &lt;1 kg/m²</th> <th>1 kg/m²≤IPWC &lt;2 kg/m²</th>	Рор	ulation included	IPWC $< -3 \text{ kg/m}^2$	-3 kg/m ² $\leq$ IPWC <-2 kg/m ²	$\begin{array}{c} -2 \text{ kg/m}^2 \leq \text{IPWC} < -1 \\ \text{kg/m}^2 \end{array}$	-1 kg/m²≤IPWC <1 kg/m²	1 kg/m ² ≤IPWC <2 kg/m ²
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. 27)         IPI < 36 months (n=1425)	Model 1ª						
$ \begin{array}{c} \mbox{IPI} < 36 \mbox{ months} (n=1425) \\ \mbox{maternal} age ≥ 35 years old "(n=265) \\ \mbox{maternal} age < 35 years old "(n=266) \\ \mbox{maternal} age < 35 years old "(n=2107) \\ \mbox{maternal} age < 35 years old "(n=2107) \\ \mbox{maternal} age < 35 years old "(n=2107) \\ \mbox{maternal} age < 35 years old "(n=266) \\ maternal$	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
$\begin{array}{c} \maternal age \geq 35 \ years of $(n=86)$ \\ maternal age < 35 \ years $(n=226)$ \\ natural age < 35 \ years $(n=226)$ \\ 0.884 (0, 33] - 2, 359 \\ 1.907 (0, 058 - 62, 300) \\ natural age < 35 \ years $(n=226)$ \\ 0.884 (0, 33] - 2, 359 \\ 1.907 (0, 167 - 2, 680) \\ 0.597 (0, 133 - 2, 675) \\ 0.646 (0, 218 - 1, 910) \\ reference \\ 1.163 (0, 589 - 2, 21) \\ 0.646 (0, 218 - 1, 910) \\ reference \\ 1.163 (0, 589 - 2, 22) \\ 0.925 (0, 473 - 1, 807) \\ reference \\ 1.163 (0, 589 - 2, 21) \\ 0.993 (0, 295 - 3, 32) \\ 0.993 (0, 218 - 2, 356) \\ 2.125 (0, 517 - 8, 744) \\ 0.595 (0, 138 - 2, 559) \\ reference \\ 1.300 (0, 870 - 2, 03) \\ reference \\ 1.300 (0, 870 - 2, 03) \\ reference \\ 1.300 (0, 870 - 2, 03) \\ reference \\ 1.300 (0, 870 - 2, 03) \\ reference \\ 1.300 (0, 870 - 2, 03) \\ reference \\ 1.300 (0, 870 - 2, 03) \\ reference \\ 1.300 (0, 813 - 3, 50) \\ reference \\ 1.301 (0, 823 - 2, 13) \\ reference \\ 1.301 (0, 823 - 2, 13) \\ reference \\ 1.301 (0, 823 - 2, 13) \\ reference \\ 1.301 (0, 823 - 2, 13) \\ reference \\ 1.301 (0, 823 - 2, 13) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.438 (1, 006 - 2, 00) \\ reference \\ 1.438 (1, 006 - 2, 00) \\ reference \\ 1.438 (1, 006 - 2, 00) \\ reference \\ 1.438 (1, 006 - 2, 00) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.438 (1, 006 - 2, 01) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, 883 - 2, 31) \\ reference \\ 1.442 (0, $	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
$\begin{array}{c} \maternal age < 35 \ {\rm years}^{\mu} & 0.\ 884 \ (0.\ 331-2.\ 359) & 1.\ 014 \ (0.\ 413-2.\ 493) & 0.\ 748 \ (0.\ 403-1.\ 389) & {\rm reference} & 1.\ 396 \ (0.\ 975-1.\ 997 \ (0.\ 132-2.\ 559) & {\rm reference} & 1.\ 103 \ (0.\ 589-2.\ 218) \\ \mbox{Without GDM}^{\mu} \ (n=2107) & 1.\ 008 \ (0.\ 288-3.\ 523) & 0.\ 987 \ (0.\ 333-2.\ 925) & 0.\ 925 \ (0.\ 473-1.\ 807) & {\rm reference} & 1.\ 537 \ (1.\ 027-2.\ 397 \ (0.\ 138-2.\ 559) & {\rm reference} & 1.\ 537 \ (1.\ 027-2.\ 397 \ (0.\ 138-2.\ 559) & {\rm reference} & 1.\ 537 \ (1.\ 027-2.\ 397 \ (0.\ 595 \ (0.\ 138-2.\ 559) & {\rm reference} & 1.\ 537 \ (1.\ 027-2.\ 397 \ (0.\ 993 \ (0.\ 295-3.\ 397 \ (0.\ 138-2.\ 559) & {\rm reference} & 1.\ 330 \ (0.\ 870-2.\ 027 \ (0.\ 877-2.\ 397 \ (0.\ 138-2.\ 559) & {\rm reference} & 1.\ 330 \ (0.\ 870-2.\ 027 \ (0.\ 877-2.\ 397 \ (0.\ 138-2.\ 559) & {\rm reference} & 1.\ 331 \ (0.\ 870-2.\ 027 \ (0.\ 877-2.\ 397 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 997-2.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \ (0.\ 993 \$	mate old [‡]	ernal age≥35 years [∉] (n=86)	1.907 (0.058-62.300)	_ *	3. 559 (0. 549– 23. 055)	reference	3.710 (0.760-18.10
GDM# (n=265)0. 670 (0. 167-2. 680)0. 597 (0. 133-2. 675)0. 646 (0. 218-1. 910)reference1. 163 (0. 589-2. 24)Without GDM# (n=2107)1. 008 (0. 288-3. 523)0. 987 (0. 333-2. 925)0. 925 (0. 473-1. 807)reference1. 537 (1. 027-2. 36)overweight or obese # (n=218)0. 649 (0. 179-2. 356)2. 125 (0. 517-8. 744)0. 595 (0. 138-2. 559)reference0. 993 (0. 295-3. 32)Normal weight # (n=1620)1. 257 (0. 320-4. 931)0. 397 (0. 108-1. 459)0. 93 (0. 491-1. 763)reference1. 300 (0. 870-2. 02)underweight # (n=534)-*-*-*reference1. 703 (0. 813-3. 50)Model 2 *IPI > 36 months (n=947)1. 107 (0. 321-3. 816)1. 009 (0. 291-3. 498)0. 620 (0. 255-1. 508)reference1. 331 (0. 823-2. 13)IPI < 36 months (n=4425)	mate (n=2	ernal age < 35 years [#] 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
Without GDM# (n=2107)1. 008 (0. 288-3. 523)0. 987 (0. 333-2. 925)0. 925 (0. 473-1. 807)reference1. 537 (1. 027-2. 337)overweight or obese # (n=218)0. 649 (0. 179-2. 356)2. 125 (0. 517-8. 744)0. 595 (0. 138-2. 559)reference0. 993 (0. 295-3. 337)Normal weight # (n=1620)1. 257 (0. 320-4. 931)0. 397 (0. 108-1. 459)0. 93 (0. 491-1. 763)reference1. 330 (0. 870-2. 037)underweight # (n=534)-*-*-*reference1. 703 (0. 813-3. 567)Iodel 2 bIPI ≥ 36 months (n=947)1. 107 (0. 321-3. 816)1. 009 (0. 291-3. 498)0. 620 (0. 255-1. 508)reference1. 442 (0. 883-2. 337)Iodel 2 bIPI ≥ 36 months (n=947)1. 107 (0. 321-3. 816)1. 009 (0. 291-3. 498)0. 620 (0. 255-1. 508)reference1. 442 (0. 883-2. 337)Iodel 2 bIPI ≥ 36 months (n=947)1. 107 (0. 321-3. 816)1. 009 (0. 291-3. 498)0. 620 (0. 255-1. 508)reference1. 442 (0. 883-2. 337)Iodel 2 bIPI ≥ 36 months (n=947)1. 107 (0. 321-3. 816)1. 009 (0. 291-3. 498)0. 620 (0. 255-1. 508)reference1. 442 (0. 883-2. 337)Imaternal age ≥ 35 years old # (n=86)0. 803 (0. 046-13. 873)-*1. 597 (0. 310-8. 218)reference1. 442 (0. 683-2. 027)GDM# (n=265)0. 694 (0. 178-2. 714)0. 616 (0. 140-2. 714)0. 582 (0. 200-1. 691)reference1. 424 (0. 627-2. 337)Without GDM# (n=2107)0. 831 (0. 244-2. 832)0. 981 (0. 339-2. 834)0. 871 (0. 449-1. 689)reference1. 542 (1. 036-2. 27)overweight or	GDM	M [#] (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
overweight or obese # (n=218)0. 649 (0. 179 - 2. 356)2. 125 (0. 517 - 8. 744)0. 595 (0. 138 - 2. 559)reference0. 993 (0. 295 - 3. 32)Normal weight # (n=1620)1. 257 (0. 320 - 4. 931)0. 397 (0. 108 - 1. 459)0. 93 (0. 491 - 1. 763)reference1. 330 (0. 870 - 2. 02)underweight # (n=534)-*-*-*reference1. 703 (0. 813 - 3. 56)fodel 2 bIPI ≥ 36 months (n=947)1. 107 (0. 321 - 3. 816)1. 009 (0. 291 - 3. 498)0. 620 (0. 255 - 1. 508)reference1. 331 (0. 823 - 2. 13)IPI < 36 months (n=1425)	With	nout 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
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. 02) underweight " (n=534) - * - * reference 1. 703 (0. 813-3. 56) todel 2 b IPI $\geq$ 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. 14) IPI $\leq$ 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. 33) maternal age $\geq$ 35 years old " (n=86) maternal age $<$ 35 years " (n=2286) 0. 803 (0. 046-13. 873) - * 1. 597 (0. 310-8. 218) reference 2. 144 (0. 544-8. 44) (n=2286) 0. 843 (0. 326-2. 177) 0. 994 (0. 409-2. 412) 0. 703 (0. 379-1. 301) reference 1. 224 (0. 627-2. 33) Without GDM [#] (n=2107) 0. 831 (0. 244-2. 832) 0. 981 (0. 339-2. 834) 0. 871 (0. 449-1. 689) reference 1. 224 (0. 627-2. 33) Without GDM [#] (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. 00) underweight " (n=534) - * - * reference 1. 930 (0. 954-3. 92)	over (n=2	weight or obese [#] 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
underweight # (n=534)- *- *- *reference1. 703 (0. 813-3.54)todel 2 bIPI > 36 months (n=947)1. 107 (0. 321-3. 816)1. 009 (0. 291-3. 498)0. 620 (0. 255-1. 508)reference1. 331 (0. 823-2. 14)IPI < 36 months (n=1425)	Nor	mal 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
fodel 2*IP1 $\geq$ 36 months (n=947)1. 107 (0. 321-3. 816)1. 009 (0. 291-3. 498)0. 620 (0. 255-1. 508)reference1. 331 (0. 823-2. 14)IP1 < 36 months (n=1425)	unde	erweight [#] (n=534)	_ *	_ *	_ *	reference	1. 703 (0. 813–3. 567
IP1 $\geq$ 36 months (n=947)1. 107 (0. 321-3. 816)1. 009 (0. 291-3. 498)0. 620 (0. 255-1. 508)reference1. 331 (0. 823-2. 14)IP1 < 36 months (n=1425)	1odel 2 ^b						
IPI < 36 months (n=1425)	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
maternal age ≥35 years old $\#$ (n=86) maternal age <35 years $\#$ (n=2286)0. 803 (0. 046-13. 873) 0. 843 (0. 326-2. 177)- *1. 597 (0. 310-8. 218) 0. 994 (0. 409-2. 412)reference2. 144 (0. 544-8. 44) 0. 703 (0. 379-1. 301)GDM# (n=265)0. 694 (0. 178-2. 714) 0. 694 (0. 178-2. 714)0. 616 (0. 140-2. 714) 0. 616 (0. 140-2. 714)0. 582 (0. 200-1. 691) 0. 582 (0. 200-1. 691)reference1. 224 (0. 627-2. 32) 0. 582 (1. 036-2. 24)Without GDM# (n=2107)0. 831 (0. 244-2. 832) (n=218)0. 981 (0. 339-2. 834)0. 871 (0. 449-1. 689) 0. 691 (0. 164-2. 913)reference1. 224 (0. 395-3. 79) 1. 224 (0. 395-3. 79)overweight or obese $\#$ (n=218)0. 736 (0. 218-2. 487) 1. 038 (0. 274-3. 925)2. 490 (0. 646-9. 590) 0. 386 (0. 107-1. 400)0. 845 (0. 446-1. 600) 0. 845 (0. 446-1. 600)reference1. 314 (0. 863-2. 00) 1. 930 (0. 954-3. 90)underweight $\#$ (n=534)- *- *- *- *- *reference1. 930 (0. 954-3. 90)	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
Inatematage < 35 years (n=2286) $0.843 (0.326-2.177)$ $0.994 (0.409-2.412)$ $0.703 (0.379-1.301)$ reference $1.438 (1.008-2.01)$ GDM# (n=265) $0.694 (0.178-2.714)$ $0.616 (0.140-2.714)$ $0.582 (0.200-1.691)$ reference $1.224 (0.627-2.39)$ Without GDM# (n=2107) $0.831 (0.244-2.832)$ $0.981 (0.339-2.834)$ $0.871 (0.449-1.689)$ reference $1.542 (1.036-2.29)$ overweight or obese # (n=218) $0.736 (0.218-2.487)$ $2.490 (0.646-9.590)$ $0.691 (0.164-2.913)$ reference $1.224 (0.395-3.79)$ normal weight # (n=1620) $1.038 (0.274-3.925)$ $0.386 (0.107-1.400)$ $0.845 (0.446-1.600)$ reference $1.314 (0.863-2.00)$ underweight # (n=534) $-*$ $-*$ $-*$ $-*$ $-*$ $-*$	mate old [#]	ernal age $\geq$ 35 years [#] (n=86)	0.803 (0.046-13.873)	_ *	1. 597 (0. 310–8. 218)	reference	2.144 (0.544-8.446
GDM# (n=265) $0.694(0.178-2.714)$ $0.616(0.140-2.714)$ $0.582(0.200-1.691)$ reference $1.224(0.627-2.38)$ Without GDM# (n=2107) $0.831(0.244-2.832)$ $0.981(0.339-2.834)$ $0.871(0.449-1.689)$ reference $1.542(1.036-2.24)$ overweight or obese # (n=218) $0.736(0.218-2.487)$ $2.490(0.646-9.590)$ $0.691(0.164-2.913)$ reference $1.224(0.395-3.79)$ normal weight # (n=1620) $1.038(0.274-3.925)$ $0.386(0.107-1.400)$ $0.845(0.446-1.600)$ reference $1.314(0.863-2.00)$ underweight # (n=534) $-*$ $-*$ $-*$ $-*$ reference $1.930(0.954-3.90)$	(n=2	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
Without GDM# (n=2107) $0.831(0.244-2.832)$ $0.981(0.339-2.834)$ $0.871(0.449-1.689)$ reference $1.542(1.036-2.24)$ overweight or obese # (n=218) $0.736(0.218-2.487)$ $2.490(0.646-9.590)$ $0.691(0.164-2.913)$ reference $1.224(0.395-3.79)$ normal weight # (n=1620) $1.038(0.274-3.925)$ $0.386(0.107-1.400)$ $0.845(0.446-1.600)$ reference $1.314(0.863-2.00)$ underweight # (n=534) $-*$ $-*$ $-*$ $-*$ reference $1.930(0.954-3.90)$	GDN	M [#] (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
overweight or obese #       0. 736 (0. 218-2. 487)       2. 490 (0. 646-9. 590)       0. 691 (0. 164-2. 913)       reference       1. 224 (0. 395-3. 79)         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. 00)         underweight # (n=534)       - *       - *       - *       reference       1. 930 (0. 954-3. 90)	With	nout 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
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. 00)         underweight # (n=534)       - *       - *       - *       reference       1. 930 (0. 954-3. 90)	over (n=2	weight or obese [#] 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
underweight [#] (n=534) - * - * reference 1.930 (0.954-3.90	norm	nal 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
	unde	erweight [#] (n=534)	_ *	_ *	_ *	reference	1.930 (0.954-3.905

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pregnancy. IPWC: interpregnancy weight change; IPI: interpregnancy interval; GDM: gestational diabetes mellitus;

5	607	OR: Odds Ratio; CI: confidence interval.
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		For peer review only - http://bmiopen.hmi.com/site/about/quidelines.yht

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OR: Odds Ratio; CI: confidence interval.

Women with one or more pregnancies in Peking university Shenzhen Hospital from Jan 2013 to Feb 2021 (n=35,675)

Women with two consecutive pregnancies (n=3,037)

Women included into this study (n=2,372)

-3 kg/m²≤IPWC<-2 kg/m² (n=57) -2 kg/m²≤IPWC<-1 kg/m² (n=183)

-1 kg/m²≤IPWC<1 kg/m² (n=1,105)

1 kg/m²≤IPWC<2 kg/m² (n=486) 2 kg/m²≤IPWC<3 kg/m² (n=264)

IPWC<-3 kg/m2 (n=48)

IPWC≥3 kg/m² (n=229)



Excluded due to: Women with a parity of one (n=32,479) Women with a parity of three or more (n=50) Women with unknown number of pregnancies (n=109)

#### Excluded due to:

Women with type 1 or type 2 diabetes (n=13) Women with delivery before 28 gestational weeks (n=9) Women with unknown or not stated BMI of the first or the second pregnancy(n=643)

209x296mm (300 x 300 DPI)

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	-

Table S1 Collinearity analysis of the independent variables

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

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	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	]
Non-adjusted OR value	1.582	1.108	0.81	reference	1.309	1.249	
OR adjusted by IPI	1.598	1.142	0.832	reference	1.288	1.253	
Percentage of the OR change	1.01%	3.07%	2.72%	-	-1.60%	0.32%	
OR adjusted by maternal age ^a	1.643	1.067	0.816	reference	1.346	1.321	
Percentage of the OR change	3.86%	-3.70%	0.74%	-	2.83%	5.76%	
OR adjusted by nationality	1.581	1.109	0.808	reference	1.311	1.246	
Percentage of the OR change	-0.06%	0.09%	-0.25%	-	0.15%	-0.24%	
OR adjusted by newborn sex ^a	1.578	1.109	0.809	reference	1.309	1.246	
Percentage of the OR change	-0.25%	0.09%	-0.12%	-	0.00%	-0.24%	
OR adjusted by GDM ^a	1.172	0.982	0.836	reference	1.375	1.238	
Percentage of the OR	-25.92%	-11.37%	3.21%	-	5.04%	-0.88%	
OR adjusted by HDCP ^a	1.569	1.083	0.809	reference	1.306	1.242	
Percentage of the OR change	-0.82%	-2.26%	-0.12%	-	-0.23%	-0.56%	
OR adjusted by macrosomia ^a	1.566	1.092	0.809	reference	1.316	1.248	
Percentage of the OR change	-1.01%	-1.44%	-0.12%	-	0.53%	-0.08%	
OR adjusted by preterm birth ^a	1.59	1.089	0.811	reference	1.299	1.242	
Percentage of the OR change	0.51%	-1.71%	0.12%	6	-0.76%	-0.56%	
OR adjusted by CS ^a	1.566	1.115	0.798	reference	1.319	1.252	
Percentage of the OR	-1.01%	0.63%	-1.48%	4	0.76%	0.24%	
OR adjusted by BMI ^a	0.906	0.837	0.718	reference	1.398	1.229	
Percentage of the OR	-42.73%	-24.46%	-11.36%	-	6.8%	-1.6%	
OR adjusted by maternal age in the	1.641	1.06	0.825	reference	1.336	1.326	
second pregnancy			1.050/	_	2.06%	6 16%	

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

IPWC  $\geq 3$ 

1.777

1.743

-1.91%

1.862

4.78%

1.776

-0.06%

1.774

-0.17%

1.782

0.28%

1.775

-0.11%

1.757

-1.13%

1.787

0.56%

1.771

-0.34%

1.835

3.26%

1.869

5.18%

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Table S3 Adjusted OR values of five IPWC categories for	or the GDM risk in the second pregnat	ding ng fo	total and in stratified analysis

7						
8 9				adjusted OR (95% CI)*	inary Ensei	
10 11		IPWC <-1 kg/m ²	-1 kg/m ² ≤IPWC <1 kg/m ²	1 kg/m ² ≤IPWC <2 kg/m ²	2 kg/m²≤IPW a b kg/m²	IPWC $\geq 3 \text{ kg/m}^2$
12 13	In total (n=2372)	0.790(0.502-1.243)	reference	1.443(1.026-2.031)	1.221(0.7950 B 800)	1.818(1.194-2.768)
14 15	IPI $\geq$ 36 months (n=947)	0.786(0.400-1.544)	reference	1.334(0.824-2.159)	1.514(0.856 295 295 297)	1.422(0.758-2.669)
16 17	IPI < 36 months (n=1425)	0.786(0.421-1.469)	reference	1.438(0.880-2.348)	0.839(0.42	2.208(1.249-3.902)
18 10	maternal age≥35 years old [#] (n=86)	0.886(0.211-3.727)	reference	2.147(0.548-8.403)	n htt ₋≗inir	1.614(0.228-11.410)
19 20 21	maternal age < 35 years [#] (n=2286)	0.789(0.488-1.273)	reference	1.439(1.009-2.054)		1.851(1.201-2.851)
22	GDM [#] (n=265)	0.619(0.280-1.369)	reference	1.226(0.628-2.396)	0.914(0.40 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.	1.723(0.752-3.946)
23 24	Without GDM [#] (n=2107)	0.886(0.512-1.533)	reference	1.542(1.036-2.296)	1.373(0.83 (2.2 73)	1.867(1.140-3.056)
25	overweight or obese $\#$ (n=218)	0.991(0.411-2.390)	reference	1.202(0.392-3.687)	1.611(0.48 <b>6</b> 5.3 <b>8</b> )	1.814(0.521-6.315)
20 27	normal weight # (n=1620)	0.749(0.428-1.309)	reference	1.314(0.863-2.000)	1.256(0.7552.028)	1.929(1.170-3.183)
28	underweight # (n=534)	_ a	reference	1.930(0.954-3.905)	0.722(0.19 ² , 2.6 ⁹ , 6)	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; GPM, gestational diabetes mellitus; OR: Odds Ratio; CI: confidence interval.

second pregnancy		
variables	adjusted OR#	95% CI#
IPWC categories interacted with IPI categories		
IPWC < -3 kg/m ² interacted with IPI $\geq$ 36 months	1.649	0.272-10.006
-3 kg/m ² $\leq$ IPWC <-2 kg/m ² interacted with IPI $\geq$ 36 months	1.313	0.220-7.822
-2 kg/m ² $\leq$ IPWC <-1 kg/m ² interacted with IPI $\geq$ 36 months	0.635	0.199-2.027
-1 kg/m ² $\leq$ IPWC <1 kg/m ² interacted with IPI $\geq$ 36 months	reference	reference
1 kg/m ² $\leq$ IPWC $\leq$ 2 kg/m ² interacted with IPI $\geq$ 36 months	0.956	0.482-1.898
$2 \text{ kg/m}^2 \leq \text{IPWC} < 3 \text{ kg/m}^2 \text{ interacted with IPI} \geq 36 \text{ months}$	1.788	0.727-4.396
IPWC $\geq$ 3 kg/m ² interacted with IPI $\geq$ 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 $\geq$ 35 years old [*]	0.458	0.026-8.014
-3 kg/m ² $\leq$ IPWC <-2 kg/m ² interacted with maternal age $\geq$ 35 years old [*]		
s	a	a
-2 kg/m ² $\leq$ IPWC $<$ -1 kg/m ² interacted with maternal age $\geq$ 35 years old [*]	2.236	0.365-13.706
-1 kg/m ² $\leq$ IPWC $<$ 1 kg/m ² interacted with maternal age $\geq$ 35 years old*	reference	reference
1 kg/m ² $\leq$ IPWC $\leq$ kg/m ² interacted with maternal age $\geq$ 35 years old*	1.514	0.345-6.647
$2 \text{ kg/m}^2 \leq \text{IPWC} < 3 \text{ kg/m}^2 \text{ interacted with maternal age } \geq 35 \text{ years old}^*$	<u>_a</u>	<u>_a</u>
IPWC $\geq 3$ kg/m ² interacted with maternal age $\geq 35$ 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
$-3 \text{ kg/m}^2 \leq \text{IPWC} \leq -2 \text{ kg/m}^2 \text{ interacted with GDM}^*$	0.651	0.106 - 4.007
$-2 \text{ kg/m}^2 < \text{IPWC} < -1 \text{ kg/m}^2 \text{ interacted with GDM}^*$	0.681	0.195-2.381
-1 kg/m ² <ipwc <1="" kg="" m<sup="">2 interacted with GDM[*]</ipwc>	reference	reference
$1 \text{ kg/m}^2 \leq \text{IPWC} \leq 2 \text{ kg/m}^2 \text{ interacted with GDM}^*$	0.779	0.359 - 1.687
$2 \text{ kg/m}^2 \leq \text{IPWC} \leq 3 \text{ kg/m}^2 \text{ interacted with GDM}^*$	0.670	0.260 - 1.727
$IPWC > 3 \text{ kg/m}^2$ interacted with GDM*	0.917	0.351-2.398
IPWC categories interacted with the BMI categories of the first trimester [*]		
$IPWC < -3 \text{ kg/m}^2$ interacted with BMI < 18.5 kg/m ^{2*} ^s	_a	a
-3 kg/m ² <ipwc <-2="" kg="" m<sup="">2 interacted with BMI &lt; 18.5 kg/m^{2*}[§]</ipwc>	_a	_a
$-2 \text{ kg/m}^2 \leq \text{IPWC} \leq -1 \text{ kg/m}^2$ interacted with BMI $\leq 18.5 \text{ kg/m}^{2*\text{ s}}$	a	_a
$-1 \text{ kg/m}^2 < \text{IPWC} < 1 \text{ kg/m}^2 \text{ interacted with BMI} < 18.5 \text{ kg/m}^2$	reference	reference
$1 \text{ kg/m}^2 \leq \text{IPWC} \leq 2 \text{ kg/m}^2 \text{ interacted with BMI} \leq 18.5 \text{ kg/m}^2 \approx$	1, 465	0, 646-3, 323
$2 \text{ kg/m}^2 \leq 12 \text{ kg/m}^2$ interacted with BMI < 18.5 kg/m ² *	0.550	0.136-2.222
$IPWC > 3 \text{ kg/m}^2$ interacted with BMI < 18.5 kg/m ² *	0.770	0.255-2.328
$IPWC < -3 \text{ kg/m}^2$ interacted with BMI > 24 kg/m ² *	0.572	0.200 2.020 0.095-3.452
$-3 \text{ kg/m}^2 < \text{IPWC} < -2 \text{ kg/m}^2 \text{ interacted with BMI } 24 \text{ kg/m}^2$	5 663	0.897-35.759
$-2 \text{ kg/m}^2 < \text{IPWC} < -1 \text{ kg/m}^2$ interacted with BMI > 24 kg/m ² *	0 741	0. 153-3 603
$-1 \text{ kg/m}^2 < \text{IPWC} < 1 \text{ kg/m}^2 \text{ interacted with BMI} > 24 \text{ kg/m}^2$	reference	reference
$1 \text{ kg/m}^2 \leq \text{IPWC} \leq 2 \text{ kg/m}^2 \text{ interacted with RMI > } 24 \text{ kg/m}^2$	0 955	0 283-3 217
$2 \text{ kg/m}^2 = 24 \text{ kg/m}^2$ interacted with BMI > $24 \text{ kg/m}^2$	1 260	0 330-4 805
$2 \text{ kg/m} = 1 \text{ kg/m}^2$ interacted with BMI > $24 \text{ kg/m}^2$	0.953	0.242 - 3.744
* in the first pregnance: # adjusted by DMI of the first trimester and (	DM in the first presson	

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

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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 i	n the first pregnancy.	

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## **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
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<b>Primary Subject Heading</b> :	Obstetrics and gynaecology
Secondary Subject Heading:	Obstetrics and gynaecology
Keywords:	Diabetes in pregnancy < DIABETES & ENDOCRINOLOGY, OBSTETRICS, Weight Gain, Maternal medicine < OBSTETRICS, Risk Factors

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1       The impact of interpregnancy weight change on the risk of         2       gestational diabetes mellitus during a second pregnancy in Chinese         3       population: a retrospective cohort study         4       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} 6       'Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China.         9       'Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen, Guangdong, China.         11       'Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases, Shenzhen, Guangdong, China.         13       'Intelligent Hospital Research Academy, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China.         14       'Guangdong, China.         15       'Ao Yang, Ying Wang and Yuzhen Liu contributed equally to this article.         16       Correspondence         17       Shlin Zhong, Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital,         18       120 Lianhua Road, Shenzhen 518036, Guangdong, China.         19       Email: Zhongshlin2013@163.com         20       Objectives This study aimed to investigate the impact of interpregnancy weight changes (IPWC)         21       Abstract         22       Objectives This study aimed to investigate the impact of interpregnancy weight changes (IPWC	2		
1       The impact of interpregnancy weight change on the risk of         2       gestational diabetes mellitus during a second pregnancy in Chinese         3       population: a retrospective cohort study         4       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} 6       'Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Shenzhen,         7       'Center of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen,         9       Junstitue of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen,         10       Guangdong, China.         9       'Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen,         11       'Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases,         12       Shenzhen, Guangdong, China.       ''Ao Yang, Ying Wang and Yuzhen Lin contributed equally to this article.         13       'Anotyang, Ying Wang and Yuzhen Lin contributed equally to this article.       Correspondence         13       'Abilin Zhong, Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital,       1120 Lianhua Road, Shenzhen 518036, Guangdong, China.         14       Email: zhongshlin2013@163.com       ''''''''''''''''''''''''''''''''''''	3		
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2       gestational diabetes mellitus during a second pregnancy in Chinese         8       population: a retrospective cohort study         11       4         12       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} 13       6         14       7         15       7         16       1         17       1         18       9         19       1         10       1         11       1         12       1         13       1         14       1         15       7.0         16       1         17       1         18       1         19       10         10       10         11       12         12       13         13       11         14       12         15       7.0         16       12         17       14         18       12.0         19       12         111       12         111       12         112 </th <th>5</th> <th></th> <th></th>	5		
3       population: a retrospective cohort study         11       4         12       5         13       6         14       6         15       7         16       1         17       1         18       6         19       2         19       1         10       1         11       3         12       1         13       1         14       1         15       7         16       1         17       1         18       1         19       2         11       3         11       3         11       3         12       3         13       4         14       1         15       4         16       1         17       4         18       1120 Lianhua Road, Shenzhen Jeacodeny, Peking University Shenzhen Hospital,         19       1120 Lianhua Road, Shenzhen 518036, Guangdong, China.         11       1120 Lianhua Road, Shenzhen 518036, Guangdong, China.         11 <t< th=""><th>7</th><th>2</th><th>gestational diabetes mellitus during a second pregnancy in Chinese</th></t<>	7	2	gestational diabetes mellitus during a second pregnancy in Chinese
<ul> <li>population: a retrospective cohort study</li> <li>Ao Yang^{1,2,3+}, Ying Wang^{1,2,3+}, Yuzhen Liu^{1,2,3+}, Juan Yang^{1,2,3}, Chang Xu⁴, Shilin Zhong^{1,2,3}</li> <li>¹² Ao Yang^{1,2,3+}, Ying Wang^{1,2,3+}, Yuzhen Liu^{1,2,3+}, Juan Yang^{1,2,3}, Chang Xu⁴, Shilin Zhong^{1,2,3}</li> <li>¹³ ¹Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China.</li> <li>¹⁴ ¹Institute of Obstetrics and Gynecology for Early Diagnosis of Major Gynecologic Diseases, Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases, Shenzhen, Guangdong, China.</li> <li>¹³ Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases, Shenzhen, Guangdong, China.</li> <li>¹⁴ Intelligent Hospital Research Academy, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China.</li> <li>¹⁵ Ao Yang, Ying Wang and Yuzhen Liu contributed equally to this article.</li> <li><b>Correspondence</b></li> <li>¹⁸ Shilin Zhong, Center of Obstetries and Gynecology, Peking University Shenzhen Hospital,</li> <li>¹¹ 1120 Lianhua Road, Shenzhen 518036, Guangdong, China.</li> <li>¹⁸ Email: zhongshilin2013@163.com</li> <li>¹⁹ <b>Abstract</b></li> <li><b>Objectives</b> This study aimed to investigate the impact of interpregnancy weight changes (IPWC) on the gestational diabetes mellitus (GDM) in the second pregnancy.</li> <li>¹⁹ <b>Design</b> A retrospective cohort study.</li> <li>¹⁰ <b>Stiting</b> Data were collected in Peking University Shenzhen Hospital from 2013 Jan to 2021 Feb.</li> <li>¹¹ <b>Participants</b> Women who had two consecutive singleton deliveries after 28 gestational weeks (N=2372).</li> <li>¹⁰ <b>Outcomes</b> The GDM in the second pregnancy (s-GDM).</li> <li>¹¹ <b>Methods:</b> 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 14g/m³ to &lt;1 kg/m²</li> <li>¹³ a sther reference. Adjusted odds ratics (aOR8) with 95% Cl statiation fform m</li></ul>	8		
4       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} 7 ¹ Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Shenzhen,         8 ¹ Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen,         9 ¹ Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen,         9 ¹ Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen,         9 ¹ Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases,         11 ³ Shenzhen, Guangdong, China.         11 ⁴ Intelligent Hospital Research Academy, Peking University Shenzhen Hospital, Shenzhen,         12 ⁴ Ao Yang, Ying Wang and Yuzhen Liu contributed equally to this article.         13 ⁴ Intelligent Hospital Research Academy, Peking University Shenzhen Hospital,         14       1120 Lianhua Road, Shenzhen 518036, Guangdong, China.         15 ⁴ Ao Yang, Ying Wang and Yuzhen Liu (GDM) in the second pregnancy weight changes (IPWC)         16       Objectives This study aimed to investigate the impact of interpregnancy weight changes (IPWC)         17       Shilinz Zhong Center of Deking University Shenzhen Hospital from 2013 Jan to 2021 Feb.         18       Participants Women who had two consecutive singleton deliveries after 28 gestational weeks <td< th=""><th>9 10</th><th>3</th><th>population: a retrospective cohort study</th></td<>	9 10	3	population: a retrospective cohort study
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<ul> <li>3 No Fang Y, Fing Wang Y, Fuziken Latt Y, Juan Fang Y, Chang Ku, Jinim Zhong Y.</li> <li>i 'Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Shenzhen,</li> <li>9 'Institute of Obstetrics and Gynecology, Shenzhen PKU-HKUST Medical Center, Shenzhen,</li> <li>10 Guangdong, China.</li> <li>11 'Shenzhen Key Laboratory on Technology for Early Diagnosis of Major Gynecologic Diseases,</li> <li>12 Shenzhen, Guangdong, China.</li> <li>13 'Intelligent Hospital Research Academy, Peking University Shenzhen Hospital, Shenzhen,</li> <li>14 Guangdong, China.</li> <li>15 'Ao Yang, Ying Wang and Yuzhen Liu contributed equally to this article.</li> <li>16 Correspondence</li> <li>17 Shilin Zhong, Center of Obstetries and Gynecology, Peking University Shenzhen Hospital,</li> <li>1120 Lianhua Road, Shenzhen 518036, Guangdong, China.</li> <li>113 Email: zhongshilin2013@163.com</li> <li>20</li> <li>21 Abstract</li> <li>22 Objectives This study aimed to investigate the impact of interpregnancy weight changes (IPWC) on the gestational diabetes mellitus (ODM) in the second pregnancy.</li> <li>23 Design A retrospective cohort study.</li> <li>24 Bersing Data were collected in Peking University Shenzhen Hospital from 2013 Jan to 2021 Feb.</li> <li>24 Participants Women who had two consecutive singleton deliveries after 28 gestational weeks (N=2372).</li> <li>24 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 &lt;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.</li> <li>25 Results: In the overall analysis, s-GDM was found to be significantly associated with IPWC value (aOR 1.111; 95%cCI 1.038-1.190) and an IPWC category of ≥</li></ul>	12	4	Ao Vangl23* Ving Wangl23* Vuzhan Liul23* Juan Vangl23 Chang Vu4 Shilin Zhangl23
<ul> <li>¹⁴ ¹⁶ ¹Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital, Shenzhen,</li> <li>¹⁷ ¹⁷ ¹⁷ ¹⁷ ¹⁷ ¹⁷ ¹⁸ ¹⁸ ¹⁸ ¹⁸ ¹⁸ ¹⁸ ¹⁸ ¹⁸</li></ul>	13	5	Ao rang /*, ring wang /*, ruzhen Liu /*, Juan rang /*, Chang Au, Shinin Zhong /*
<ul> <li>Guangdong, China.</li> <li>¹⁷ Center of Obstetries and Gynecology, Fexing University Shenzhen Hospital, Shenzhen,</li> <li>¹⁸ ¹⁸ ¹⁸ ¹⁸ ¹⁸ ¹⁸ ¹⁸ ¹⁸</li></ul>	14 15	0	Contar of Obstatries and Cymanology Daking University Shanzhan Hagnital Shanzhan
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2716Correspondence2817Shilin Zhong, Center of Obstetrics and Gynecology, Peking University Shenzhen Hospital,29181120 Lianhua Road, Shenzhen 518036, Guangdong, China.30Email: zhongshilin2013@163.com3119Email: zhongshilin2013@163.com322033343421Abstract3622Objectives This study aimed to investigate the impact of interpregnancy weight changes (IPWC)3723on the gestational diabetes mellitus (GDM) in the second pregnancy.3824Design A retrospective cohort study.3924Design A retrospective cohort study.3025Setting Data were collected in Peking University Shenzhen Hospital from 2013 Jan to 2021 Feb.4126Participants Women who had two consecutive singleton deliveries after 28 gestational weeks4227(N=2372).4329Methods: IPWC was defined as the change in BMI between the first trimester of the second4430pregnancy and that of the first pregnancy, categorized into four groups with -1 kg/m² to <1 kg/m²4831as the reference. Adjusted odds ratios (aORs) with 95% CIs attained from multivariable logistic4925regression were used to assess the association between IPWC and s-GDM, in both total subjects4136as thatified subgroups.4243as thatified subgroups.4344354435453646304730	26	15	*Ao Yang, Ying Wang and Yuzhen Liu contributed equally to this article.
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4411111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111111 <th>43</th> <td>28</td> <td><b>Outcomes</b> The GDM in the second pregnancy (s-GDM).</td>	43	28	<b>Outcomes</b> The GDM in the second pregnancy (s-GDM).
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53 55 (aUK 1.111, 95%CI 1.058-1.190) and an IPWC category $OI \ge 3$ kg/m ² (aUK 1.821; 95%CI 1.197- 54 36 2.772). In the stratified analysis, the significant association between IPWC $\ge 3$ kg/m ² and s-GDM	52	54 25	(a) $D = 1.111, 0.59/CL = 1.028, 1.100)$ and an $DWC$ established for $2 \ln^2 (200, 1.821, 0.59/CL = 1.07)$
$36  2.7/2$ ). In the stratified analysis, the significant association between IPWC $\ge 3$ kg/m ² and s-GDM	53	35	(aOK 1.111; 95%C1 1.038-1.190) and an IPWC category of $\ge 3$ kg/m ⁻ (aOK 1.821; 95%C1 1.197-
	54 55	36	2.1/2). In the stratified analysis, the significant association between IPWC $\geq$ 3 kg/m ² and s-GDM
56 37 was evident only in the subgroups of an inter-pregnancy interval (IPI) of less than 36 months	56	37	was evident only in the subgroups of an inter-pregnancy interval (IPI) of less than 36 months
57 38 (aOR 2.210, 95%CI 1.251-3.904), under the age of 35 (aOR 1.854, 95%CI 1.204-2.857), non-	57	38	(aOK 2.210, 95%CI 1.251-3.904), under the age of 35 (aOK 1.854, 95%CI 1.204-2.857), non-
58 39 diabetic status in the first pregnancy (f-ND) (aOR 1.872, 95%CI 1.143-3.065), and those with	58 50	39	diabetic status in the first pregnancy (f-ND) (aOR 1.872, 95%CI 1.143-3.065), and those with
40 normal weight in the first pregnancy (f-NW) (aOR 1.936, 95%Cl 1.174-3.193). The significant	60	40	normal weight in the first pregnancy (f-NW) (aOR 1.936, 95%CI 1.174-3.193). The significant

41 association between IPWC value and s-GDM was also showed only in these subgroups (P < 0.05).

42 In f-DN subgroup, even an IPWC category of 1 kg/m² to <3 kg/m² was significantly associated 43 with s-GDM (aOR 1.486, 95%CI 1.044-2.117). IPWC < -1 kg/m² was not significantly associated

44 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 46 women with an IPI less than 36 months, those under 35 years old, non-diabetic individuals, or 47 those with normal weight during their first pregnancy. The potential influence of prior GDM on 48 the relationship between IPWC and s-GDM warrants further investigation.

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

### 51 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  $\ge 3 \text{ kg/m}^2$  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 <  $-1 \text{ kg/m}^2$  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.

### 4 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 weight², diet³, maternal age⁴, exercise, and genetics⁵. 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 GDM⁸.

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 review¹⁷ 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  $\geq$ 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

 that current GDM diagnostic criteria in China were recommended by the IADPSG in 2010¹⁸, 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 GDM²⁰. 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).

### 98 MATERIALS ADN METHODS

#### 99 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.

### 108 Patient and Public Involvement statement

109 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/m²), was categorized into four groups: <-1 kg/m², -1 kg/m² to <1kg/m² (considered as stable BMI and used as a reference), 1 kg/m² to <3 kg/m², and  $\geq 3$  kg/m²²⁴. BMI level in the first pregnancy (f-BMI) was classified into four categories: underweight (f-UW) (<18.5 kg/m²), normal weight (f-NW) (18.5 kg/m² to <24.0 kg/m²), and overweight or obese (f-OB) ( $\geq$ 24.0 kg/m²). 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 122 consecutive pregnancies ²³. Advanced maternal age (AMA) was described as being 35 years or
 123 older ²⁵, and young maternal age (YMA) was defined as the age less than 35 years old.

124 The primary outcome of the study was the GDM in the second pregnancy (s-GDM). 125 Throughout the entire study period, GDM was diagnosed using the IADPSG criteria²⁶, which 126 involved a 75-gram oral glucose tolerance test. According to these criteria, a diagnosis of GDM 127 was made if the serum blood glucose levels were  $\geq$ 5.1 mmol/L at 0 hour, and/or  $\geq$ 10.0 mmol/L at 128 1 hour, and/or  $\geq$ 8.5 mmol/L at 2 hours, between 24-28 weeks of gestation.

#### 129 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). 

#### 139 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  $\pm$  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 ( $\geq$ 36 months, < 36 months²⁷), 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**

### 155 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).

160 During the first pregnancy, the participants' average age was  $28.25 \pm 3.33$  years, with a mean 161 BMI of  $20.48 \pm 2.64$  kg/m² and an average delivery gestational age of  $38.82 \pm 1.53$  weeks. 162 Instances of f-GDM occurred in 265 cases (11.17%). The prevalence of f-GDM among subjects

164

respectively.

1 2 3

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

5	164	respectively.
6	165	The median IPWC for all participants was 0.725 kg/m ² (P25: -0.240 kg/m ² ; P75: 1.770
7	166	kg/m ² ). Figure 2A illustrates the distribution of four IPWC categories. Subjects with an IPI of 36
8	167	months or more had a higher proportion of IPWC ranging from 1 to $< 3 \text{ kg/m}^2$ ( $P = 0.001$ ) and a
9 10	168	lower proportion of stable IPWC compared to those with an IPI of less than 36 months ( $P = 0.008$ .
11	169	Figure 2B) There was no significant difference in the proportions of all four IPWC categories
12	170	between those with and without f GDM ( $P > 0.05$ Figure 2C). Compared to women with f UW a
13	170	between mose with and without 1-ODM ( $1 > 0.05$ , 1 igure 2C). Compared to wonten with 1-OW, a
14	1/1	Target percentage of women with 1-OB had an IP wC of less than -1 kg/m ( $F < 0.001$ , Figure 2D),
15	172	while a smaller percentage had an IPwC of 2-3 kg/m ² ( $P < 0.001$ , Figure 2D).
17	173	During the second pregnancy, the participants had an average age of $31.15 \pm 3.57$ years. The
18	174	mean BMI was $21.27 \pm 2.90$ kg/m ² , and the average gestational age at delivery was $38.54 \pm 1.45$
19	175	weeks. Notably, 303 participants, accounting for 12.77% of the total, were diagnosed with s-GDM.
20	176	Comparison of IPWC and other risk factors between s-CDM and s-ND groups
22	170	In the s-GDM group, the IPWC value maternal age f-BML s-BML and IPL were all
23	170	in the s-obbit group, the first value, inaternal age, 1-Divit, s-Divit, and fit were an eignificantly higher compared to the s ND group ( $B < 0.01$ Table 1). Moreover, the percentage of
24	1/8	significantly higher compared to the s-ND group ( $P < 0.01$ , Table 1). Moreover, the percentage of
25	179	participants with IPWC $\ge 3$ kg/m ² , f-GDM, f-HDCP, f-CS, f-AMA, f-OB, and IPI $\ge 36$ months
26 27	180	was notably greater in the s-GDM group than in the s-ND group ( $P < 0.01$ , Table 1). Conversely,
28	181	the proportion of subjects with a stable IPWC ( $-1 \text{ kg/m}^2$ to $<1 \text{ kg/m}^2$ ) and f-UW was significantly
29	182	lower in the s-GDM group than in the s-ND group ( $P < 0.05$ , Table 1).
30	183	The effect of IPWC on s-CDM in total subjects
31	105	Following universible and collingerity angly as (Supplementary Table 1) verifields such as
33	104	IDI f DML maternal ago (f MA) f CDM f HDCP f magrogamia f DTP, and f CS ware included
34	105	iPI, I-DMI, maternal age (I-MA), I-ODM, I-HDCP, I-macrosonna, I-PTB, and I-CS were included
35	186	in Model 1. Subsequently, f-BMI and f-GDM were incorporated into Model 2 due to their notable
36	187	impact on the effect of IPWC in bivariable analyses. In both adjusted models (Model 1 and Model
37	188	2), the IPWC value was significantly positively associated with s-GDM, while this association
39	189	was marginal in the unadjusted model ( <i>P</i> =0.05, Table 2).
40	190	In both unadjusted and adjusted models, an IPWC of $\ge 3 \text{ kg/m}^2$ was independently linked to
41	191	an increased risk of s-GDM compared to the reference IPWC (Table 2). Moreover, Model 2
42	192	revealed that an IPWC ranging from 1 kg/m ² to $<3$ kg/m ² was also linked to a heightened risk of
43	193	s-GDM. In contrast, other IPWC categories, such as IPWC < -1 kg/m ² , demonstrated no
45	194	significant association with s-GDM (Table 2).
46		
47	195	The effect of IPWC on s-GDM in stratified analysis
48 40	196	In alignment with the unadjusted model, both Model 1 and Model 2 demonstrated a
50	197	significant association between the IPWC value and an increased risk of s-GDM within the f-
51	198	YMA, f-ND, and f-NW subgroups (Table 3). Furthermore, both Model 1 and Model 2 indicated a
52	199	significant correlation between the IPWC value and s-GDM in subgroups with an IPI of less than
53 54	200	36 months, whereas this relationship was not observed in the unadjusted model (Table 3).
55	201	However, the IPWC value did not correlate significantly with s-GDM in subgroup of IPI $\geq$ 36
56	202	months, as well as in the f-AMA, f-GDM, f-OB, or f-UW subgroups (Table 3). Additionally, there
57	203	was no significant interaction between IPWC value and the four stratification factors ( $P > 0.05$
58	204	Table 3)
59 60	201	$IPWC \ge 3 \text{ kg/m}^2$ was significantly correlated with an increased risk of s CDM for
00	205	II WC > 5 Kg/III was significantly conclated with all increased fisk of s-ODM 101

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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  $\ge$  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  $1 \text{ kg/m}^2$  to  $<3 \text{ kg/m}^2$  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).

#### 220 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  $\geq 3$ 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  $\ge 3 \text{ kg/m}^2$  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-GDM²⁸. Participants who experienced an increase in BMI had higher odds of developing s-GDM compared to those whose BMI remained unchanged²⁹. 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 al⁹. and Knight-Agarwal et al³⁰. 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

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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 pregnancy³¹. 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 GDM⁸. Insulin resistance plays a crucial role in the development of GDM among individuals who are overweight³². 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 prepregnancy weights³³. Moreover, substantial weight gain before pregnancy has also been found to be associated with GDM³⁴. Some observational studies^{12,13, 35, 36} and two systematic reviews^{16,37} have suggested that even IPWC categories  $\geq 1 \text{ kg/m}^2$  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 criteria³⁶, diverse diagnostic standards for GDM^{12,13, 35, 36}, differing definitions of IPWC³⁵, 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.

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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  $\geq 3 \text{kg/m}^2$  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  $\geq$  36 months was associated with a higher risk of weight gain from the first to the second pregnancy³⁸. Previous studies have also shown that women with GDM tend to gain weight faster before pregnancy compared to non-GDM women³⁹. Therefore, it would be more reasonable to investigate the association between weight change and s-GDM within a narrower range of IPI9. Tano et al. 's study suggested that annual BMI gain was associated with the risk of GDM during the subsequent pregnancy⁴⁰. 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  $\ge 3 \text{ kg/m}^2$  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 293 25 to 29 years old ⁴¹. Additionally, the risk of GDM in Asian women was more strongly correlated 294 with age starting at 25 years old, compared to Europid women⁴². Regrettably, no other stratified 295 studies based on maternal age were identified in the existing literature. This finding has important 296 implications in establishing weight control goals based on age. To further validate this hypothesis, 297 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 $\ge$  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  $\geq 4$  units ⁴³. Conversely, without GDM in their first pregnancy, an IPWC >1 unit heightened their GDM risk in the second pregnancy⁴³. 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  $\leq 1 \text{ kg/m}^2$  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 risk⁴⁵. 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.

S8 335 Certainly, this study has several limitations. Firstly, it is a retrospective, single-center study,
 S9 336 with all data collected from historical databases. Some confounding factors, such as diet, family

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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.

#### 342 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  $\ge 3 \text{ kg/m}^2$ . 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).

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#### **Competing interests** None declared.

**Patient consent for publication** Not required.

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

- **Provenance and peer review** Not commissioned; externally peer reviewed.
- **Data availability statement** Data are available upon reasonable request.

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4 5	508	Figure 1 Flow chart showing inclusion and exclusion in this study <i>BMI</i> hody mass index: <i>IPWC</i>
с С	509	interpresentation weight change
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9	511	Figure 2 The frequencies of the IPWC categories and their distributions in different subgroups <i>The</i>
10	512	frequencies of four IPWC categories showed right-skewed (A); Subgroup of IPI $\geq$ 36 months owned a larger proportion of IPWC 1 to <
11	513	3 kg/m ² and a smaller proportion of stable IPWC (B); The proportion of four IPWC categories did not differ between f-GDM and f-ND
12	514	group (C); Overweight or obese women owned a larger proportion of IPWC $< -1$ kg/m ² and a smaller proportion of IPWC of 1 kg/m ² to $<$
13 14	515	3 kg/m ² (D).IPWC: interpregnancy weight change; IPI: inerpregnancy interval; GDM: gestational diabetes mellitus; UW: underweight;
14	516	NW: normal weight: OB: overweight or obese: f.: in the first pregnancy
16	510	In normal weight, OD. over weight of obese, j In the just pregnancy.
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risk factors	s-GDM group $(n=202)$	s-ND group $(n=2060)$	difference of mean (
continuous variables	(11=303)	(11-2009)	(95% CI) 10f S-GI
$IBWC [kg/m^2 (interquartile range)]$	0.070( 0.150.2.110)	0.680( 0.250 1.730)	0 221/0 000 0 44
f MA (years)	20 20+2 52	0.080(-0.250-1.750)	1 184(0 785 1 59
f DML $(1/2)$	$29.29 \pm 3.33$	$26.10\pm 3.28$	1.104(0.705-1.50
$\frac{1-DMI}{(kg/m^2)}$	$21.55 \pm 5.02$	$20.30\pm 2.33$	0.903(0.004-1.32
S-Divit (kg/iii-)	$22.50\pm 3.51$	$21.12\pm2.01$	1.104(0.791-1.37
antagorical variables	30.10(20.07-48.33)	50.95(22.25-40.25)	4.398(2.379-0.21
$\leq -1 kg/m^2$	32(10.56)	253(12,23)	0 848(0 574-1 25
$1 kg/m^2 t_0 < 1 kg/m^2$	52(10.50) 124(40.92)	233(12.23) 984(47.56)	0.848(0.574-1.25
$1 \text{ kg/m}^2 \text{ to } < 3 \text{ kg/m}^2$	124(40.92) 105(34.65)	645(31.17)	1 171(0 908 1 51)
$3 kg/m^2$	105(54.05)	187(0.04)	1.171(0.908-1.31)
$\geq$ 5 kg/m ²	42(13.80)	10((9.04)	1.020(1.131-2.31)
f A PT $[n (9/)]$	289(93.38)	1900(93.02)	1.001(0.011-1.91
f CDM [n (%)]	20(0.00)	100(4.83)	0.994(7.425.13.1)
$f \text{ HDCP } [\pi (\%)]$	20((41.38)	(1(2,05))	9.004(7.425-15.1
$\begin{array}{c} \text{I-HDCP} \left[ \Pi \left( \% \right) \right] \\ \text{f here otherweidiens } \left[ \Pi \left( \% \right) \right] \end{array}$	20(0.00)	01(2.95)	2.320(1.383-3.91
f har arthur idian [n (%)]	14(4.02)	118(5.70)	0.801(0.454-1.41
$f = A D S \left[ \frac{1}{2} \left( \frac{9}{2} \right) \right]$	2(0.66)	16(0.77)	0.855(0.195-5.72
$1-APS [\Pi (\%)]$	0(0.00)	4(0.19)	-
I-SLE[n(%)]	0(0.00)	12(0.58)	-
I-PPH [n (%)]	8(2.64)	34(1.64)	1.623(0.744-3.54
f = PCOS[n(%)]	2(0.66)	4(0.19)	3.43(0.626-18.80
1-CS[fi(%)]	125(41.25)	610(29.48)	1.00(1.311-2.15)
$\begin{bmatrix} I - P \ I \ B \ [\Pi (\%)] \end{bmatrix}$	23(7.59)	108(5.22)	1.492(0.935-2.38
f male newherm $[n (\%)]$	18(3.94)	01(3.91)	1.55(0.910-2.02
	140(40.04)	1033(49.93)	0.938(0.732-1.21
I-AMA £ UW	24(7.92)	02(3.00)	2.785(1.710-4.55
I-UW f OD	49(10.17)	465(25.44)	0.701(0.505-0.97
I-OD	50(10.50) 152(50.17)	705(28,42)	2.000(1.456-2.92
IP1 ≥ 30 months	152(50.17)	195(38.42)	1.013(1.200-2.05
518 f: in previous pregnancy; s: in the s	econd pregnancy; the corre	esponding IPWC category	was analyzed as binary
519 variable; MA: maternal age; BMI:	body mass index; IPWC: in	terpregnancy weight changed	ge; IPI: interpregnancy
520 interval; ART: assisted reproducti	ve technology; GDM: ges	tational diabetes mellitus;	HDCP: hypertensive
521 disorder complicating pregnancy; A	APS: antiphospholipid syndr	ome; SLE: systemic lupu	s erythematosus; PPH:
522 postpartum hemorrhage; PCOS: pol	ycystic ovary syndrome; CS	: cesarean section; PTB: p	reterm birth; OR: odds
523 ratio; CI: confidence interval.			
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534	Table 2	The effect of IPV	WC on the GDM	in the second preg	nancy in una	diusted and adjusted	
535	models		unadjusted OR (95%	adjusted OR (	95% CI)	adjusted OR (95% CI)	
-	IPWC value	e	<u>CI)</u> 1.067(1.000-1.139)	1.105(1.029	-1.186)	1111(1.038-1.190)	
	IPWC cates	zories	1.007(1.000 1.109)	1.105(1.02)	1.100)	1.111(1.020 1.170)	
	<-1 k	$g/m^2$	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	referen	ce	reference	
	1 kg/i	$m^2$ to < 3 kg/m ²	1.292(0.978-1.706)	1.350(0.996	-1.832)	1.364(1.009-1.842)	
	$\geq 3 \text{ kg}$	g/m ²	1.782(1.215-2.615)	1.797(1.173	-2.754)	1.821(1.197-2.772)	
536	IPWC: int	erpregnancy weight	change; GDM: gesta	tional diabetes mellitu	s. * adjusted b	y IPI, f-BMI, f-AMA, f-	
537	GDM, f-H	DCP, f-macrosomia,	f-PTB, and f-CS; # ad	djusted by f-BMI and f	-GDM.		
538	- 3	.,,	,,				
539	Table 3	3 The effect of IPV	WC value on the G	DM in the second r	pregnancy in	stratified subgroups	
		unadiusted	model	Model 1*	<u> </u>	Model 2 [#]	¥
Population	included	OR	P for	adjusted OR	P for	adjusted OR	P for
		(95% CI)	interaction	(95% CI)	interaction	(95% CI)	interacti
IPI≥36 mont	hs (n=947)	1.069(0.970-1.180)		1.091(0.984-1.210)		1.097(0.990-1.215)	
IPI < 36 mont	hs	1 055(0 0(( 1 154)	0.846	0.885	0.885	1 11((1 015 1 225)	0.968
(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=22	86)	1.08(1.010-1.156)	0.701	1.11(1.032-1.194)	0.002	1.12(1.043-1.202)	0.970
f-GDM (n=26	5)	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)	
$f \cap P(n-218)$		1 070(0 042 1 225)		1 002(0 041 1 271)		1 092(0 029 1 249)	
f NW (n - 162)	າງ	1.079(0.943-1.233)	) 0.926	1.093(0.941-1.271)	0.082	1.082(0.938-1.248)	0.027
$f_{-1}W (n=534)$	) \	1.090(1.011-1.100) 1.126(0.952-1.332)	0.920	1.084(0.882-1.331)	0.982	1.120(1.035-1.228) 1.105(0.924-1.322)	0.927
540	n: in prov	ious programaw: IDW	) VC: interprogrammy y	1.084(0.882-1.331)	torprognanav i	1.105(0.924-1.522)	
540	p. In prev	ious pregnancy, ir w	vC. Interpregnancy v	vergin change, IFI. In	nelliter ND	nervai, AlviA. auvanceu	
541	maternal a	age; YMA: young n	naternal age; GDM:	gestational diabetes i	nemius; ND:	non-diabetic status; OB:	
542	overweigh	t or obese; NW: nori	mal weight; UW: und	lerweight. adjusted by	y IPI, f-BMI, f-	AMA, f-GDM, f-HDCP,	
543	f-macroso	mia, f-PTB, and f-CS	; # adjusted by f-BMI	and f-GDM.			
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Dopulation included	OR (95% CI)					
Population included	$< -1 \text{ kg/m}^2$	-1 kg/m ² to < 1 kg/m ²	$1 \text{ kg/m}^2 \text{ to} < 3 \text{ kg/m}^2$	$\geq 3 \text{ kg/m}^2$		
unadjusted model						
IPI $\geq$ 36 months (n=947)	1.151(0.630-2.103)	reference	1.470(0.990-2.184)	1.618(0.908-2.8		
IPI < 36 months (n=1425)	0.893(0.505-1.581)	reference	1.052(0.704-1.572)	1.886(1.129-3.1		
f-AMA (n=86)	0.972(0.263-3.595)	reference	1.591(0.483-5.237)	1.458(0.236-8.9		
f-YMA (n=2286)	0.984(0.636-1.525)	reference	1.323(0.992-1.766)	1.852(1.249-2.7		
f-GDM (n=265)	0.764(0.355-1.644)	reference	1.039(0.591-1.827)	1.718(0.760-3.8		
f-ND (n=2107)	1.036(0.604-1.774)	reference	1.463(1.028-2.082)	1.831(1.119-2.9		
f-OB (n=218)	0.882(0.395-1.967)	reference	1.200(0.529-2.724)	1.964(0.646-5.9		
f-NW (n=1620)	0.885(0.529-1.481)	reference	1.294(0.923-1.815)	1.777(1.119-2.8		
f-UW (n=534)	10.	reference	1.554(0.823-2.936)	1.849(0.739-4.6		
Model 1*						
IPI $\geq$ 36 months (n=947)	0.851(0.429-1.685)	reference	1.446(0.943-2.216)	1.417(0.751-2.6		
IPI < 36 months (n=1425)	0.872(0.464-1.639)	reference	1.272(0.816-1.984)	2.298(1.287-4.1		
f-AMA (n=86)	1.298(0.265-6.365)	reference	1.710(0.418-6.987)	3.230(0.394-26.4		
f-YMA (n=2286)	0.838(0.515-1.363)	reference	1.362(0.994-1.866)	1.813(1.170-2.8		
f-GDM (n=265)	0.643(0.287-1.444)	reference	1.058(0.589-1.900)	1.770(0.759-4.1		
f-ND (n=2107)	0.965(0.552-1.686)	reference	1.522(1.063-2.179)	1.900(1.151-3.1		
f-OB (n=218)	0.860(0.342-2.160)	reference	1.218(0.464-3.196)	2.050(0.549-7.6		
f-NW (n=1620)	0.834(0.475-1.464)	reference	1.319(0.914-1.904)	1.907(1.148-3.1		
f-UW (n=534)	-	reference	1.415(0.702-2.854)	1.394(0.480-4.0		
Model 2 [#]						
IPI $\geq$ 36 months (n=947)	0.782(0.398-1.537)	reference	1.396(0.915-2.131)	1.422(0.757-2.6		
IPI < 36 months (n=1425)	0.799(0.428-1.494)	reference	1.208(0.780-1.871)	2.210(1.251-3.9		
f-AMA (n=86)	0.808(0.193-3.389)	reference	1.390(0.382-5.055)	1.790(0.255-12.		
f-YMA (n=2286)	0.798(0.494-1.289)	reference	1.395(1.022-1.905)	1.854(1.204-2.8		
f-GDM (n=265)	0.623(0.282-1.376)	reference	1.096(0.618-1.943)	1.722(0.752-3.9		
f-ND (n=2107)	0.901(0.520-1.559)	reference	1.486(1.044-2.117)	1.872(1.143-3.0		
f-OB (n=218)	0.992(0.411-2.394)	reference	1.367(0.553-3.380)	1.815(0.521-6.3		
f-NW (n=1620)	0.760(0.435-1.330)	reference	1.296(0.901-1.864)	1.936(1.174-3.1		
f-UW (n=534)	-	reference	1.575(0.804-3.084)	1.472(0.549-3.9		

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

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559 560 561	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.





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

209x296mm (300 x 300 DPI)



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.

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251x172mm (300 x 300 DPI)

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	-

Supplementary Table 1 Collinearity analysis of the independent variables

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;

s-GDM risk				
variables	adjusted OR*	95% CI*		
IPWC categories interacted with IPI categories				
IPWC < -1 kg/m ² interacted with IPI $\geq$ 36 months	0.756	0.396-1.442		
-1 kg/m ² $\leq$ IPWC <1 kg/m ² interacted with IPI $\geq$ 36 months	reference	reference		
1 kg/m ² $\leq$ IPWC <3 kg/m ² interacted with IPI $\geq$ 36 months	1.393	0.951-2.042		
IPWC $\geq$ 3 kg/m ² interacted with IPI $\geq$ 36 months	1.322	0.715-2.440		
IPWC categories interacted with f-AMA				
IPWC $< -1 \text{ kg/m}^2$ interacted with s-AMA	0.707	0.156-3.21		
-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 $\geq$ 3 kg/m ² interacted with f-AMA	1.603	0.205-12.51		
IPWC categories interacted with f-GDM				
$IPWC < -1 \text{ kg/m}^2$ interacted with f-GDM	0.618	0 278-1 37		
$-1 \text{ kg/m}^2$ (IPWC <1 kg/m ² interacted with f-GDM	reference	reference		
$1 \text{ kg/m}^2 \leq \text{IPWC} \leq 3 \text{ kg/m}^2$ interacted with f-GDM	0 984	0 550-1 761		
$IPWC \ge 3 \text{ kg/m}^2 \text{ interacted with f-GDM}$	1.602	0.691-3.71		
IPWC categories interacted with the BMI categories of the first trime	ster			
$11 \text{ wC} < -1 \text{ kg/m}^2$ interacted with f-U w	-	-		
$-1 \text{ kg/m}^2 \le 1P \text{ wC} < 1 \text{ kg/m}^2$ interacted with 1-U w	reference	reference		
1 kg/m ² $\leq$ 1PWC $\leq$ 3 kg/m ² interacted with 1-UW	1.144	0.668-1.96		
IPWC $\geq 3 \text{ kg/m}^2$ interacted with t-UW	1.145	0.458-2.858		
IPWC < $-1$ kg/m ² interacted with f-OB	0.794	0.358-1.762		
-1 kg/m ² $\leq$ IPWC <1 kg/m ² interacted with f-OB	reference	reference		
$1 \text{ kg/m}^2 \leq IPWC \leq 3 \text{ kg/m}^2$ interacted with f-OB	1.213	0.530-2.776		
IPWC $\geq$ 3 kg/m ² interacted with f-OB	1.820	0.533-6.212		

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f-BMI, f-AMA, f-GDM, f-HDCP, f-macrosomia, f-PTB, and f-CS.

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#### 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.

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