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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 gestational diabetes mellitus (GDM) in the second pregnancy.

Design A single-centre retrospective cohort study was conducted in China.

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

Participants Participants include women who had two consecutive singleton deliveries after 28 gestational weeks (n=2372).

Outcomes The GDM in the second pregnancy (s-GDM) was set as the outcome.

Methods IPWC was defined as the change in body mass index between the first trimester of the second pregnancy and that of the first pregnancy, categorised into four groups with −1 kg/m² to <1 kg/m² as the reference. Adjusted ORs (aORs) with 95% CIs attained from multivariable logistic regression were used to assess the association between IPWC and s-GDM, in both total subjects and stratified subgroups.

Results In the overall analysis, s-GDM was found to be significantly associated with IPWC value (aOR 1.111; 95% CI 1.038 to 1.190) and an IPWC category of ≥3 kg/m² (aOR 1.821; 95% CI 1.197 to 2.772). In the stratified analysis, the significant association between IPWC ≥3 kg/m² and s-GDM was evident only in the subgroups of an interpregnancy interval (IPI) of less than 36 months (aOR 2.210, 95% CI 1.251 to 3.904), under the age of 35 (aOR 1.854, 95% CI 1.204 to 2.857), non-diabetic status in the first pregnancy (f-ND) (aOR 1.872, 95% CI 1.143 to 3.065) and those with normal weight in the first pregnancy (aOR 1.936, 95% CI 1.174 to 3.193). The significant association between IPWC value and s-GDM was also shown only in these subgroups (p<0.05). In f-DN subgroup, even an IPWC category of 1 kg/m² to <3 kg/m² was significantly associated with s-GDM (aOR 1.486, 95% CI 1.044 to 2.117). IPWC < −1 kg/m² was not significantly associated with s-GDM either in the overall analysis or in the stratified analysis (p>0.05).

Conclusion An IPWC of 3 kg/m² or higher may increase the risk of s-GDM, particularly among women with an IPI of less than 36 months, those under 35 years old, individuals without diabetes, or those with normal weight during their first pregnancy. The potential influence of prior GDM on the relationship between IPWC and s-GDM warrants further investigation.

STRENGTH AND LIMITATIONS OF THIS STUDY

⇒ The association between interpregnancy weight changes (IPWC) and second pregnancy gestational diabetes mellitus (s-GDM) was examined in a cohort of 2372 cases involving consecutive singleton births in China.
⇒ Both the IPWC value and an IPWC ≥3 kg/m² were significantly associated with s-GDM, as demonstrated by two multivariable logistic regression models. Stratified analysis revealed that these associations were present only in women with interpregnancy interval <36 months, maternal age <35 years old, without previous GDM, and those with normal weight during their first pregnancy.
⇒ This study did not reveal a significant association between IPWC < −1 kg/m² and a reduced risk of s-GDM.
⇒ The main limitation is the retrospective design, and the data of diet, family history of diabetes and gestational weight gain during the first pregnancy, were not included in the analysis.
⇒ The sample size for certain subgroups is relatively small.

INTRODUCTION

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

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

Several studies indicate a significant correlation between interpregnancy weight changes (IPWC) and GDM in the second pregnancy (s-GDM).[9–13] However, there is no consensus on the precise impact of IPWC on the risk of s-GDM. In 2019–2021, systematic analyses by Teulings *et al*,[14] Timmermans *et al*,[15] and Nagpal *et al*[16] confirmed the positive association between IPWC and s-GDM risk. Nevertheless, these studies did not find that weight loss between pregnancies reduced the s-GDM risk. Conversely, Oteng-Ntim *et al*'s systematic review[17] suggested the protective effect of reducing IPWC on s-GDM. Timmermans *et al*[15] identified that an IPWC of 1–3 kg/m² correlates with an OR of 1.64 (95% CI 1.28 to 2.11) for s-GDM, and IPWC of ≥3 kg/m² with an OR of 2.42 (95% CI 1.62 to 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 International Association of Diabetes and Pregnancy Study Groups (IADPSG) in 2010,[18] these studies' applicability to the Chinese population warrants re-evaluation. 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 (AMA; >30 years) and multiparity have increased the risk of GDM.[20] The interpregnancy period is a critical time of weight management and health improvement to reduce the risk of s-GDM.[21 22] Regardless of whether they have had diabetes in their first pregnancy, both women and their physicians are interested in determining the ideal weight management target to minimise the risk of GDM in future pregnancies. Therefore, we conducted a single-centre, retrospective study in China to analyse the impact of weight change during two pregnancies on the risk of GDM in the second pregnancy (s-GDM).

MATERIALS AND METHODS

Study design and population

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

Patient and public involvement statement

None.

Definitions of the variables and outcome

In this study involving two consecutive pregnancies, we designated the earlier pregnancy as 'the first pregnancy' and the latter as 'the second pregnancy'. The primary variable examined was IPWC, defined as the difference in BMI between the first trimester of the second pregnancy and that of the first pregnancy.[23] IPWC, expressed in BMI units (kg/m²), was categorised into four groups: <−1 kg/m², −1 kg/m² to <1 kg/m² (considered as stable BMI and used as a reference), 1 kg/m² to <3 kg/m² and ≥3 kg/m².[24] 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) (≥24.0 kg/m²). The 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 consecutive pregnancies.[23] AMA was described as being 35 years or older,[25] and young maternal age (YMA) was defined as the age less than 35 years old.

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

Data collection

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

Statistical method

The data analysis was performed using SPSS V.24.0 statistical software (IBM). Categorical variables were presented as *n* (%) and compared using the χ^2 test. Normally distributed variables were presented as mean±SD and compared using Student's t-test. Non-normally distributed variables were presented as median (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<10 in collinearity assessment. Model 2 only included the covariates which altered the OR of IPWC on s-GDM by more than 10%. Stratified analysis was performed within specific subgroups categorised by IPI (≥36 months, <36 months[27]), and the variables of previous pregnancy, such as maternal age (f-AMA and f-YMA), GDM status (f-GDM and f-ND) and BMI level (f-OB, f-NW and f-UW). Additionally, this study separately analysed the interaction between IPWC value and categories with these four stratification factors. A p value of less than 0.05 was considered statistically significant.

RESULTS

Baseline characteristics of the subjects

A total of 35 675 participants who had experienced at least one pregnancy at Peking University Shenzhen Hospital were recorded between January 2013 and February 2021. After disqualifying 33 303 participants based on the exclusion criteria, a final cohort of 2372 participants who had undergone two consecutive singleton deliveries were included (figure 1).

During the first pregnancy, the participants' average age was 28.25±3.33 years, with a mean BMI of 20.48±2.64 kg/m² and an average delivery gestational age of 38.82±1.53 weeks. Instances of f-GDM occurred in 265 cases (11.17%). The prevalence of f-GDM among subjects with f-UW, f-NW and f-OB was 8.61% (46/534), 10.19% (165/1620) and 24.77% (54/218), respectively.

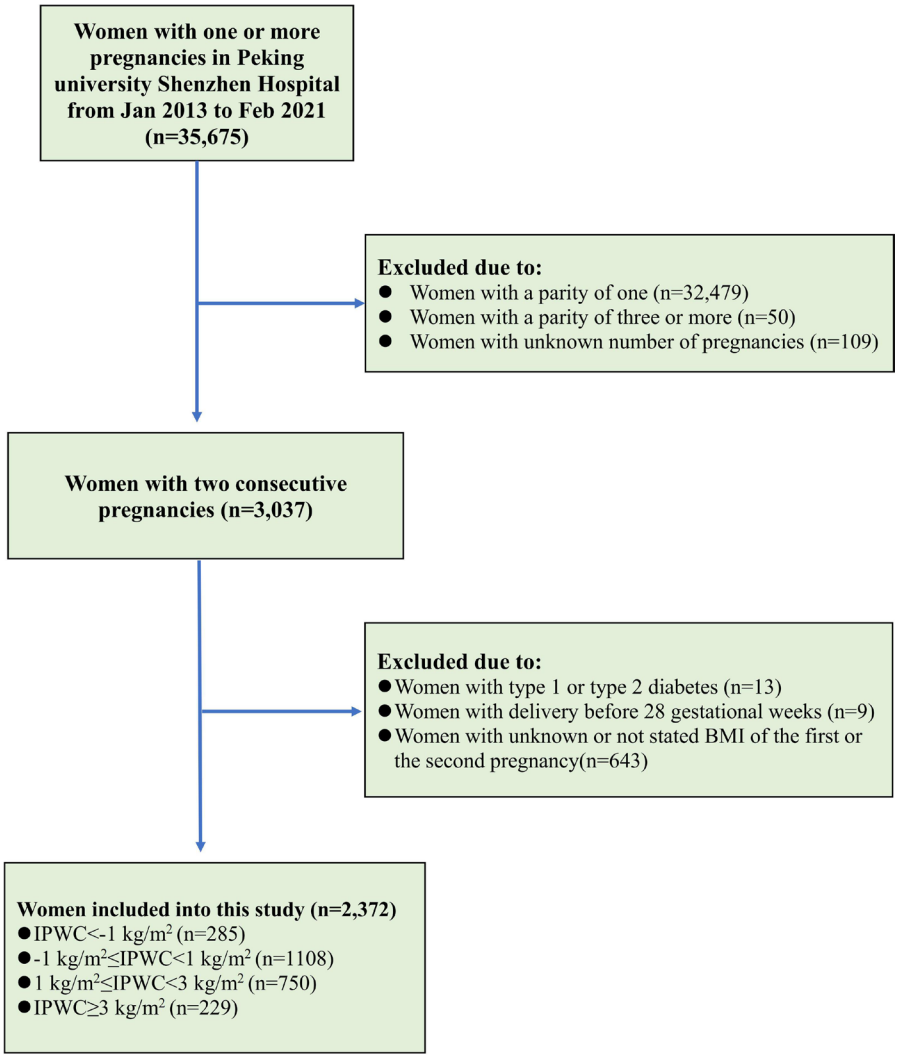

Figure 1 Flow chart showing inclusion and exclusion in this study. BMI, body mass index; IPWC, interpregnancy weight change.

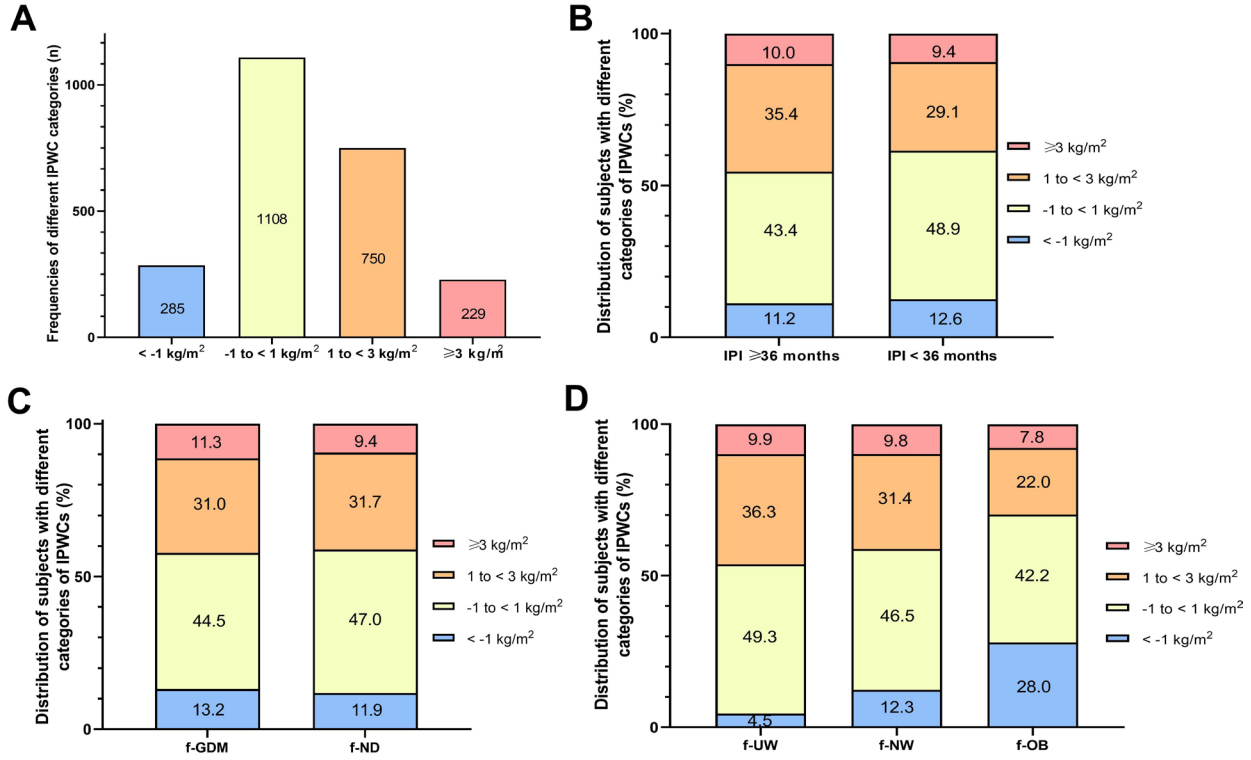

Figure 2 The frequencies of the IPWC categories and their distributions in different subgroups. The frequencies of four IPWC categories showed right-skewed (A) . Subgroup of IPI ≥36 months owned a larger proportion of IPWC 1 to <3 kg/m² and a smaller proportion of stable IPWC (B). The proportion of four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

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

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

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

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

The effect of IPWC on s-GDM in total subjects

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

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

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

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

*The corresponding IPWC category was analysed as binary variable.
†p < 0.05
‡p < 0.01
AMA, advanced maternal age; APS, antiphospholipid syndrome; ART, assisted reproductive technology; BMI, body mass index; CS, caesarean section; f, in previous pregnancy; GDM, gestational diabetes mellitus; HDCP, hypertensive disorder complicating pregnancy; IPI, interpregnancy interval; IPWC, interpregnancy weight change; MA, maternal age; OB, overweight or obese; PCOS, polycystic ovary syndrome; PPH, postpartum haemorrhage; PTB, preterm birth; s, in the second pregnancy; SLE, systemic lupus erythematosus; UW, underweight.

The effect of IPWC on s-GDM in stratified analysis

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

IPWC ≥3 kg/m² was significantly correlated with an increased risk of s-GDM for individuals with an IPI of less than 36 months, f-YMA, f-DN and f-NW, across both unadjusted models and adjusted models (models 1 and

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

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

*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.
‡p < 0.05
§p < 0.01
AMA, advanced maternal age; BMI, body mass index; CS, caesarean section; GDM, gestational diabetes mellitus; HDCP, hypertensive disorder complicating pregnancy; IPI, interpregnancy interval; IPWC, interpregnancy weight change; PTB, preterm birth.

2) (table 4). Furthermore, both unadjusted and adjusted models showed that an IPWC between 1 kg/m² and <3 kg/m² was significantly linked with s-GDM in the f-ND subgroup (table 4). Model 2 further indicated a significant association between an IPWC of 1 kg/m² to <3 kg/m² and s-GDM in the f-YMA subgroup (table 4). Conversely, no significant associations were observed between any IPWC categories and s-GDM in the subgroups of IPI ≥36 months, f-AMA, f-GDM, f-OB or f-UW (table 4). An IPWC <−1 kg/m² also showed no significant association with s-GDM across any subgroup (p>0.05). In the f-GDM subgroup, no significant difference in s-GDM incidence was found between women with an IPWC of 1 kg/m² to <3 kg/m² and those with a stable IPWC (online supplemental figure 1A). However, in the f-ND subgroup, women with an IPWC of 1 kg/m² to <3 kg/m² had a significant higher incidence of s-GDM compared with those with a stable IPWC (online supplemental figure 1B). Furthermore, no

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

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

*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.
‡p < 0.05
§p < 0.01
AMA, advanced maternal age; BMI, body mass index; CS, caesarean section; GDM, gestational diabetes mellitus; HDCP, hypertensive disorder complicating pregnancy; IPI, interpregnancy interval; IPWC, interpregnancy weight change; ND, non-diabetic status; NW, normal weight; OB, overweight or obese; p, in previous pregnancy; PTB, preterm birth; UW, underweight.; YMA, young maternal age.

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

Population included	OR (95% CI)			
	< −1 kg/m²	−1 kg/m² to <1 kg/m²	1 kg/m² to <3 kg/m²	≥3kg/m²
Unadjusted model				
IPI ≥36 months (n=947)	1.151 (0.630 to 2.103)	Reference	1.470 (0.990 to 2.184)	1.618 (0.908 to 2.883)
IPI<36 months (n=1425)	0.893 (0.505 to 1.581)	Reference	1.052 (0.704 to 1.572)	**1.886 (1.129 to 3.151)**‡
f-AMA (n=86)	0.972 (0.263 to 3.595)	Reference	1.591 (0.483 to 5.237)	1.458 (0.236 to 8.997)
f-YMA (n=2286)	0.984 (0.636 to 1.525)	Reference	1.323 (0.992 to 1.766)	**1.852 (1.249 to 2.747)**§
f-GDM (n=265)	0.764 (0.355 to 1.644)	Reference	1.039 (0.591 to 1.827)	1.718 (0.760 to 3.882)
f-ND (n=2107)	1.036 (0.604 to 1.774)	Reference	**1.463 (1.028 to 2.082)**‡	**1.831 (1.119 to 2.993)**‡
f-OB (n=218)	0.882 (0.395 to 1.967)	Reference	1.200 (0.529 to 2.724)	1.964 (0.646 to 5.966)
f-NW (n=1620)	0.885 (0.529 to 1.481)	Reference	1.294 (0.923 to 1.815)	**1.777 (1.119 to 2.820)**‡
f-UW (n=534)	–	Reference	1.554 (0.823 to 2.936)	1.849 (0.739 to 4.624)
Model 1*				
IPI≥36 months (n=947)	0.851 (0.429 to 1.685)	Reference	1.446 (0.943 to 2.216)	1.417 (0.751 to 2.675)
IPI < 36 months (n=1425)	0.872 (0.464 to 1.639)	Reference	1.272 (0.816 to 1.984)	**2.298 (1.287 to 4.104)**§
f-AMA (n=86)	1.298 (0.265 to 6.365)	Reference	1.710 (0.418 to 6.987)	3.230 (0.394 to 26.466)
f-YMA (n=2286)	0.838 (0.515 to 1.363)	Reference	1.362 (0.994 to 1.866)	**1.813 (1.170 to 2.808)**§
f-GDM (n=265)	0.643 (0.287 to 1.444)	Reference	1.058 (0.589 to 1.900)	1.770 (0.759 to 4.129)
f-ND (n=2107)	0.965 (0.552 to 1.686)	Reference	**1.522 (1.063 to 2.179)**‡	**1.900 (1.151 to 3.135)**‡
f-OB (n=218)	0.860 (0.342 to 2.160)	Reference	1.218 (0.464 to 3.196)	2.050 (0.549 to 7.659)
f-NW (n=1620)	0.834 (0.475 to 1.464)	Reference	1.319 (0.914 to 1.904)	**1.907 (1.148 to 3.170)**‡
f-UW (n=534)	–	Reference	1.415 (0.702 to 2.854)	1.394 (0.480 to 4.048)
Model 2†				
IPI≥36 months (n=947)	0.782 (0.398 to 1.537)	Reference	1.396 (0.915 to 2.131)	1.422 (0.757 to 2.669)
IPI < 36 months (n=1425)	0.799 (0.428 to 1.494)	Reference	1.208 (0.780 to 1.871)	**2.210 (1.251 to 3.904)**§
f-AMA (n=86)	0.808 (0.193 to 3.389)	Reference	1.390 (0.382 to 5.055)	1.790 (0.255 to 12.584)
f-YMA (n=2286)	0.798 (0.494 to 1.289)	Reference	**1.395 (1.022 to 1.905)**‡	**1.854 (1.204 to 2.857)**§
f-GDM (n=265)	0.623 (0.282 to 1.376)	Reference	1.096 (0.618 to 1.943)	1.722 (0.752 to 3.941)
f-ND (n=2107)	0.901 (0.520 to 1.559)	Reference	**1.486 (1.044 to 2.117)**‡	**1.872 (1.143 to 3.065)**‡
f-OB (n=218)	0.992 (0.411 to 2.394)	Reference	1.367 (0.553 to 3.380)	1.815 (0.521 to 6.327)
f-NW (n=1620)	0.760 (0.435 to 1.330)	Reference	1.296 (0.901 to 1.864)	**1.936 (1.174 to 3.193)**‡
f-UW (n=534)	–	Reference	1.575 (0.804 to 3.084)	1.472 (0.549 to 3.947)

*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.
‡p < 0.05
§p < 0.01
AMA, advanced maternal age; BMI, body mass index; f, in previous pregnancy; GDM, gestational diabetes mellitus; HDCP, hypertensive disorder complicating pregnancy; IPI, interpregnancy interval; IPWC, interpregnancy weight change; ND, non-diabetic status; NW, normal weight; OB, overweight or obese; PTB, preterm birth; UW, underweight; YMA, young maternal age.

significant interactions were observed across the various IPWC categories when analysed with the four stratification factors (p>0.05, online supplemental table 2).

DISCUSSION

This single-centre study conducted in China reveals a significant association between IPWC value and the risk of developing GDM during a second pregnancy, particularly

when IPWC is ≥3 kg/m². Stratified analysis confirmed this association for participants with an IPI of 36 months or less, maternal age under 35, no previous GDM and normal weight in their first pregnancy. In women without GDM in the first pregnancy, 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 −1 kg/m² and the decreased risk of the GDM in the second pregnancy. This study provides valuable guidance for women aiming to prevent GDM in their second pregnancy by setting weight management goals.

The study identified a significant positive effect of IPWC ≥3 kg/m² on GDM in the second pregnancy across two different models, underscoring the reliability of this finding. Over the past decade, several studies conducted in different countries have suggested a potential link between IPWC and the risk of s-GDM.[16 17] Whiteman *et al*'s study identified a significant association between changes in BMI classification, particularly from normal to overweight or obese, and the risk of s-GDM.[28] Participants who experienced an increase in BMI had higher odds of developing s-GDM compared with those whose BMI remained unchanged.[29] In addition, the magnitude of the change in BMI was also thought to be associated with s-GDM risk. Earlier investigations suggested that an IPWC 3 kg/m^2 or more increased the likelihood of developing s-GDM, when compared with the stable IPWC category (±1 kg/m^2).[11] Subsequent research by Bogaerts *et al*.[9] and Knight-Agarwal *et al*.[30] also confirmed this finding, which is consistent with the results in our study.

For IPWC of 1 kg/m² to <3 kg/m², its significant association with s-GDM was found only in model 2 but not in model 1, suggesting that the association between this category of IPWC and s-GDM needs to be further confirmed in the unstratified population. However, stratified analyses suggested that in the f-ND subgroup, both models 1 and 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 effect of f-GDM cannot be ruled out, which may help explain this difference. Women with a history of GDM have a high risk of recurrence in their next pregnancy.[31] Our study suggested that such women had a risk of GDM recurrence of more than 45% even if they maintained a stable IPWC (online supplemental figure 1), which completely masked the effect of IPWC 1 kg/m² to <3 kg/m². The large influence of GDM history may make it difficult to achieve the goal of reducing GDM risk in the second pregnancy by controlling IPWC in this population.

Being overweight or obese prior to pregnancy is a significant risk factor for GDM.[8] Insulin resistance plays a crucial role in the development of GDM among individuals who are overweight.[32] Furthermore, excessive gestational weight gain (GWG) is closely linked to the occurrence of GDM.[7 8] To mitigate the risk of GDM and macrosomia, the Institute of Medicine suggests adopting appropriate GWG guidelines for singleton pregnancies based on prepregnancy weights.[33] Moreover, substantial weight gain before pregnancy has also been found to be associated with GDM.[34] Some observational studies[10 12 13 35] and two systematic reviews[16 36] have suggested that even IPWC categories ≥1 kg/m^2 were linked to a higher risk of GDM in the second pregnancy. Variations in the association between IPWC categories and s-GDM across studies may stem from differences in population criteria,[35] diverse diagnostic standards for GDM,[10 12 13 35] differing definitions of IPWC,[10] or distinct confounding factors considered in relation to GDM.[10 13 35] 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 centred 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 Lynes *et al* (OR=1.08, 95% CI 1.05 to 1.10).[12] Therefore, we suggest that controlling IPWC to less than 3 kg/m^2 may be effective in reducing the risk of GDM in the next pregnancy in Chinese population.

Unlike the overall study results, the results of stratified analysis suggested that the impact of IPWC on s-GDM varied in different subgroups. Even with the same IPWC categories, the risk of s-GDM differs based on IPI, maternal age, GDM status or BMI in the first pregnancy. Stratified analysis revealed that IPWC categories ≥3 kg/m^2 had a more significant impact on the risk of s-GDM in participants with a shorter IPI compared with those with a longer IPI. Compared with an interval of 24–35 months, an interval ≥36 months was associated with a higher risk of weight gain from the first to the second pregnancy.[37] Previous studies have also shown that women with GDM tend to gain weight faster before pregnancy compared with non-GDM women.[38] Therefore, it would be more reasonable to investigate the association between weight change and s-GDM within a narrower range of IPI.[9] Tano *et al*'s study suggested that annual BMI gain was associated with the risk of GDM during the subsequent pregnancy.[39] 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 IPWC on s-GDM risk diminishes after 36 months between pregnancies.

In the stratified analysis by maternal age, our study identified a significant association between an IPWC of ≥3 kg/m^2 and an increased risk of s-GDM in women under 35, but not in older women. For those with AMA, 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 with women aged 25–29 years old.[40] Additionally, the risk of GDM in Asian women was more strongly correlated with age starting at 25 years old, compared with Europid women.[41] Regrettably, no other stratified studies based on maternal age were identified in the existing literature. This finding has important implications in establishing weight control goals based on age. To further validate this hypothesis, further research with a larger sample size is necessary.

Similarly, stratified analysis based on BMI during the first pregnancy revealed that the association between IPWC and s-GDM was significant only in normal-weight women, with no significant link found in those who were overweight or obese. This contrasts with the findings of McBain *et al*[6] and Ku *et al*,[35] who reported a significant relationship between IPWC and s-GDM across all BMI subgroups, with the larger IPWC category showing increased s-GDM risk particularly in the lower BMI subgroup. However, McBain *et al*[6] used the interval −2 kg/m²< IPWC < 2 kg/m² as a reference and defined overweight or obesity as BMI ≥25 kg/m², while Ku *et al*[35] used a BMI cut-off of 23 kg/m², potentially contributing to the differences in results. Given that women with overweight or obesity in our study had a higher risk of f-GDM (24.77%), we hypothesised 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 categories 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 women with overweight or obesity with GDM in their first pregnancy, the risk of GDM in a subsequent pregnancy was markedly higher if IPWC was ≥4 units.[42] Conversely, without GDM in their first pregnancy, an IPWC>1 unit heightened their GDM risk in the second pregnancy.[42] Collectively, these findings imply that IPWC has a more pronounced impact on s-GDM risk in normal-weight women compared with 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,[43] thus not elevating s-GDM risk.

Our study did not find evidence to support the protective effect of IPWC <−1 kg/m² on s-GDM, which is consistent with the findings of other studies.[12 13 30 35] We hypothesise 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 prepregnancy weight significantly reduced the risk of s-GDM in women with a BMI greater than 25 kg/m² during their first pregnancy. This effect was not observed in women with a BMI less than 25 kg/m².[36] Conversely, a systematic analysis by Kirkegaard *et al* found the opposite association: in women with a BMI less than 25 kg/m², a decrease in BMI was significantly associated with increased s-GDM risk.[44] 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 with maintaining a stable BMI.[42] These studies reveal ongoing uncertainty regarding the association between weight loss and GDM risk in different participant populations.

Certainly, this study has several limitations. First, it is a retrospective, single-centre study, with all data collected from historical databases. Some confounding factors, such as diet, family history of diabetes and GWG during the first pregnancy, were not included in the analysis, potentially impacting the results. Second, 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. Third, excluding women without BMI information may have introduced selection bias.

CONCLUSION

Our study in China revealed a clear correlation between the risk of GDM in the second pregnancy and the IPWC, specifically when the IPWC is ≥3 kg/m². 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.

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