Pre-Pregnancy Body Mass Index and Gestational Weight Gain are Associated with the Maternal-Infant Adverse Outcomes in Chinese Women with Gestation Diabetes

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Pre-pregnancy body mass index and gestational weight gain are associated with the maternal-infant adverse outcomes in Chinese women with gestation diabetes

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Abstract

The gestational weight gain (GWG) range of Chinese women with gestational diabetes mellitus (GDM) still remains unclear. Our objective was to identify the ranges of GWG in Chinese women with GDM, and to investigate the associations between pre-pregnancy body mass index (BMI), GWG and maternal-infant adverse outcomes. GDM Women delivering singleton from 2013 to 2018 in a tertiary public hospital were collected. Logistic regression analysis was used to assess the joint effects of pre-pregnancy BMI and GWG on maternal-infant adverse outcomes. Finally, 14,578 women were collected. The ranges of GWG of Chinese women with GDM in the underweight, normal weight, overweight and obese groups were 5.95-21.95kg, 4.23-21.83kg, 0.88-21.12kg and -1.76-19.95kg, respectively. The risks of large for gestational age (LGA), macrosomia and cesarean delivery were significantly increased with the increase of pre-pregnancy BMI. Furthermore, the risks of LGA, macrosomia and cesarean delivery were significantly higher in normal weight group with GWG higher than the National Academy of Medicine’s (NAM) recommendation. Similarly, in overweight group with GWG higher than NAM recommendation, the risks of LGA were significantly higher, while, the risks of macrosomia were significantly lower. In conclusion, the ranges of GWG in GDM women were different with NAM recommendation.

Introduction

Gestational diabetes mellitus (GDM) is the most common complication, threatening the health of pregnant women and their offspring. The incidence of GDM is increasing. 14.8% pregnant women in China were suffered from GDM. GDM is associated with the increased risks of maternal-infant adverse outcomes. Women with GDM have higher incidence of gestational hypertension, fetal growth restriction, premature delivery, cesarean delivery, postpartum hemorrhage, hyperinsulinemia and hypoglycemia. Moreover, GDM women are 7.5-times more likely to develop type 2 diabetes mellitus.
(T2DM) compared to women without GDM \(^7\), and their offspring are also at higher risks of developing childhood obesity \(^8\) and T2DM \(^9\). The development of GDM was associated with multiple factors. Pre-pregnant women with higher body mass index (BMI) have 4-9 times higher incidence of GDM than those of normal weight women \(^10\). Maternal obesity and higher gestational weight gain (GWG) are associated with higher risk of GDM \(^11,12\).

GWG represents the nutritional status of a pregnant woman during pregnancy. It is also an indicator of maternal fat accumulation, and the growth of the uterus, placenta and fetus\(^13\). Pre-pregnancy BMI gain also reflects maternal nutritional conditions before conception \(^3\). Abnormal GWG and pre-pregnancy BMI were both associated with pregnancy complications and maternal-infant adverse outcomes \(^14,15\). A systematic review in 196,670 pregnant women found that 47% women had GWG greater than the National Academy of Medicine’s (NAM) recommended criteria, while 23% women was below the recommended values. Women with GWG larger than the recommended ranges were associated with a higher risk of adverse maternal-infant outcomes, compared with GWG within the recommended range \(^15\). However, due to differences in race, dietary habits and culture, the recommended ranges of NAM are not suitable for Chinese women \(^16\). The appropriate ranges of GWG in women with GDM are not clear in China.

In this study, we aimed to identify the ranges of GWG for Chinese women with GDM and to investigate the associations of GWG and maternal-infant adverse outcomes in GDM women. Our analysis showed that GWG ranges in Chinese GDM women were significantly different from the criteria recommended by the NAM. We also showed that Pre-pregnancy BMI was positively associated with the high risks of LGA, macrosomia and cesarean delivery. In normal weight group, the risks of LGA, macrosomia and cesarean delivery were higher in GDM women with GWG higher than NAM recommendation.
Results

Characteristics of the GDM patients

According to the NAM guidelines, all women were divided into four groups based on the pre-pregnancy BMI. 73% (10,623 of 14,578) women were with normal BMI, while only 230 (1.6%) women were in obese group (Table 1). There were 2013 women in underweight group and 1694 women in overweight group, respectively (Table 1). The gestational BMI gain was significantly different in the four groups. The gestational BMI was mostly increased in women in underweight group (3.87±2.09). On the contrary, women in obese group had relatively lower increase of gestational BMI (2.56±2.35). The gestational BMI gain in normal weight group and overweight group was 3.68±2.02 and 2.91±2.07, respectively (Table 1).

The ranges and the rates of GWG in Chinese women with GDM is different from NAM recommended values

We also calculated the GWG in GDM women in the underweight, normal weight, overweight and obese groups. The gestational weight was mostly increased in women in underweight group (14±4.06). On the contrary, women in obese group had relatively low increase of gestational weight (9.1±5.54) (Table 2). The GWG in normal weight group and overweight group was 13.08±4.47 and 10.54±4.91, respectively (Table 2).

The GWG ranges and GWG rates in GDM women in different pre-pregnancy BMI subgroups were also tested. We found that, the Chinese GDM women had different GWG ranges in underweight, normal weight, overweight and obese groups. The underweight GDM group had the narrowest GWG ranges (from 5.95 to 21.95kg) (Table 2). Moreover, women in the underweight group had the fastest rate of GWG than other groups (Fig. 1). The ranges of GWG in the normal weight and overweight groups were from 4.23 to 21.83kg and from 0.88 to 21.12kg, respectively. On the contrary, GWG in the obese group had the widest GWG ranges (from -1.76 to 19.95kg) than normal weight, overweight and obese groups. Also obese group had the slowest and fluctuated GWG
Previously, the GWG ranges and GWG rates in four different BMI groups had been tested by NAM. So, we compared the GWG ranges and rates of Chinese GDM women with the NAM recommendation. We found that in all underweight, normal weight, overweight and obese groups, the GWG ranges in Chinese GDM women were significantly different from the criteria recommended by NAM (Table 2). Additionally, except underweight group, the rates of GWG among Chinese women with GDM were also different from those recommended by NAM (Table 2).

**Characteristics of the maternal-infant adverse outcomes of GDM patients**

GDM women are suffered many maternal-infant adverse outcomes, including LGA, SGA, prematurity, macrosomia and cesarean delivery. We found that, 10112 of out 14578 GDM women were suffered at least one of the adverse outcomes. The highest risk for GDM women was cesarean delivery. More than 36% GDM women were suffered from cesarean delivery, followed by LGA, prematurity and macrosomia adverse outcomes (Table 3).

The maternal-infant adverse outcomes were significantly different in underweight, normal weight, overweight and obese groups. Compared with other three groups, GDM women in the underweight group were more suffered from SGA. The incidence of SGA in the underweight group was 10.54% (214 of 2,031), while, the incidence of SGA in obese group was only 3.91% (9 of 230) (Table 3). On the contrary, other maternal-infant adverse outcomes, like LGA, macrosomia and cesarean delivery were most occurred in obese group. 55.22%, 21.14% and 13.04% of GDM women in the obese group were suffered from cesarean delivery, LGA or macrosomia, respectively (Table 3). The incidence of prematurity was not significantly different in underweight, normal weight, overweight and obese groups (Table 3).

Moreover, the GDM women in underweight, normal weight, overweight and obese groups were further divided into three subgroups based on the recommended GWG ranges by NAM. We found that, women in the higher than recommended GWG group
had the highest risks of adverse outcomes than the other two subgroups, whereas the lower than recommended GWG group had the lowest risks of adverse outcomes. However, in the underweight group, the equal to recommended GWG group had the lowest risks of adverse outcomes (Table 3).

**Associations of GWG with the total risks of maternal-infant adverse outcomes in each pre-pregnancy BMI subgroups**

The absolute risks for any maternal-infant adverse outcome were increased across maternal pre-pregnancy BMI and were independent of GWG (Fig. 2). The GWG ranges which were most associated with the maternal-infant outcomes in underweight, normal weight, overweight and obese groups were determined. Underweight group with GWG of 4-11kg had the lower risks of maternal-infant adverse outcomes, and women with GWG ranging between 12 and 17kg had higher risks for adverse outcomes (Fig. 3a). Women in the normal weight group with GWG of 4-10kg had lower risks for adverse outcomes, while, women with GWG ranging from 10 to 16kg had higher risks of adverse outcomes (Fig. 3b). In the overweight group and obese group, women with GWG of 0-6kg or GWG of 0-4kg had lower risks for adverse outcomes, respectively, while women with GWG of 6-11kg or more than 4kg had higher risks for adverse outcomes respectively (Fig. 3c and 3d).

**Associations of maternal pre-pregnancy BMI and GWG with maternal-infant adverse outcome**

Using Logistic regression analysis, we determined the associations of maternal pre-pregnancy BMI and GWG with each maternal-infant adverse outcome. We showed that the incidences of LGA, macrosomia, cesarean delivery and total adverse outcomes were significantly increased with the increasing of pre-pregnancy BMI ($p < 0.001$) (Table 4). On the contrary, the risk of SGA was significantly decreased with the increasing of
pre-pregnancy BMI ($p < 0.001$) (Table 4). However, the incidence of prematurity was not associated with the maternal pre-pregnancy BMI (Table 4).

Moreover, in underweight group, the incidences of LGA, prematurity, macrosomia and cesarean delivery were not correlated with the GWG. However, the risks of SGA were significantly higher in the subgroup with GWG lower than the NAM recommendation ($p < 0.001$) (Table 4). On the contrary, the incidence of total adverse outcomes was significantly higher in the subgroup with GWG higher than the NAM recommendation ($p < 0.001$) (Table 4). The risks of LGA, macrosomia, cesarean delivery were significantly higher ($p < 0.001$), while, the incidence of SGA was significantly lower ($p < 0.001$) in normal weight group with GWG higher than the NAM recommendation. However, the risks of prematurity were not associated with the GWG in normal weight group (Table 4). In overweight group, the risks of SGA, prematurity, cesarean delivery and total adverse outcomes had not significant difference in different GWG subgroups. However, the incidence of LGA was significantly higher in the subgroup above the recommended GWG ($p < 0.05$), while the risk of macrosomia were significantly higher in the subgroup below the recommended GWG ($p < 0.05$) in overweight group (Table 4). In the obese group, the incidences of LGA, SGA, prematurity, macrosomia, cesarean delivery and total adverse outcomes were all not associated with the GWG (Table 4).

**Mata-analysis of the associations of maternal-infant adverse outcomes with pre-pregnancy BMI in three independent cohorts**

At last, we determined the maternal-infant adverse outcomes in different pre-pregnancy BMI subgroups using other three independent cohorts, including normal Chinese women 17, Japanese women 18, European and North American women 14. The Chinese normal and GDM women had not significant difference in the incidences of SGA, cesarean delivery and macrosomia. However, the risks of prematurity from all pre-pregnancy BMI groups and LGA in the normal weight group and the overweight group among women with
GDM were significantly higher than those of normal Chinese women (Fig. 4a). Compared with Japanese women, the incidences of cesarean delivery and macrosomia in four pre-pregnancy BMI groups were significantly higher in GDM women. Also, in Chinese GDM women, the risks of prematurity in the normal weight group and in the overweight group were significantly higher than those of Japanese women, while the risk of prematurity in the underweight group had opposite effects (Fig. 4b). Moreover, in Chinese GDM women, the risks of LGA, prematurity and cesarean delivery in four pre-pregnancy BMI groups were significantly higher than European and North American women (Fig. 4c). On the contrary, the risks for SGA were lower than European and North American women (Fig. 4c).

**Discussion**

Considering the ethnic differences between Chinese women and women in Europe or North America, GWG should be different. Moreover, women who have better diet and more exercise during pregnancy should have lower GWG and lower risks of maternal-infants adverse outcomes. In this study, we showed a wider range of GWG among Chinese women with GDM, compared with the NAM recommended ranges. Moreover, GWG in the obese group had the widest GWG range than normal weight, overweight and obese groups.

NAM guidelines and other studies, suggested that GWG was a strong predictor of the maternal-infants adverse outcomes. Our analysis validated those results that GWG had negative correlation with maternal-infants adverse outcomes in Chinese women with GDM. Chinese women with GDM in the normal weight, overweight and obese groups experienced lower GWG was associated with lower risks of adverse outcomes. The ranges of GWG that were most associated with the low risks of maternal-infant adverse outcomes for Chinese women with GDM were 4-11kg, 4-10kg,
0-6kg, and 0-4kg for the underweight, normal weight, overweight and obese groups, respectively.

Furthermore, the risks of LGA, SGA, prematurity, macrosomia or cesarean delivery had different correlations with GWG. Similar to previous studies, the risk of LGA, macrosomia and cesarean delivery were strongly associated with the increase of pre-pregnancy BMI and GWG, particularly in the obese group. Studies and our analysis suggested that obese women with GDM had a higher incidence of LGA than the normal weight women. On the contrary, GWG lower than the NAM recommended among Chinese women with GDM was associated with a higher risk for SGA and prematurity. We also demonstrated that GWG higher than the NAM recommended was associated with a lower risk of premature birth, particular for GDM women with GWG lower than the NAM recommended in the obese group. Consistent with previous studies, pregnant women with GWG lower than the recommended value were at a higher risk of prematurely delivering. Moreover, the maternal-infant adverse outcomes in different pre-pregnancy BMI subgroups were significantly different from normal Chinese women, Japanese women, European and North American women.

To our best knowledge, this was the largest retrospective cohort study to identify the ranges and to reveal the associations of GWG and maternal-infant adverse outcomes among Chinese women with GDM. We also used maternal age, pre-pregnancy BMI and weight, and mode of delivery to adjust the significant potential confounding factors. However, there were several limitations to this study. First, this was a retrospective cohort study which may have bias because of the independent process of data collection and analysis. Second, we did not analyze the diet and physical activity of the women with GDM during their pregnancy. Finally, we only used cohorts from one hospital. Therefore, the collected data and findings may not be representative of Chinese GDM women. Next, a prospective cohort study of the ranges of GWG among GDM women from multiple centers in China should be carried out.
Methods

Study design and participants
This was a retrospective cohort study in a tertiary public maternity and children’s hospital in China. 17,216 women were diagnosed with GDM from 2013 to 2018 in our hospital. After data screening, 589 GDM women delivered more than one babies and 2059 GDM women without following up data were also excluded. Finally, 14,578 sets of data from 14,334 GDM patients were used for further studies. Participants’ information such as maternal age, occupation, maternal pre-pregnancy BMI, pre-pregnancy weight and gestational week, latest weight before childbirth, the gestational week at delivery, birth weight of neonate and maternal-infant adverse outcomes was collected. Women who had more than one singleton pregnancy were analyzed more than once.

Classification of the GDM women
All women were stratified into four weight groups based on the pre-pregnancy BMI: underweight (BMI<18.5 kg/m²), normal weight (18.5 kg/m²≤BMI<25.0 kg/m²), overweight (25.0 kg/m²≤BMI<30.0 kg/m²) and obese (BMI≥30.0 kg/m²). GDM women in each group were further divided into three subgroups based on the recommended GWG ranges by NAM: lower, equal or higher than the recommended range subgroups. GWG was defined as the weight difference between pre-pregnancy and just before delivery.

Maternal-infants adverse outcomes
The maternal-infants adverse outcomes included large for gestational age (LGA), small for gestational age (SGA), prematurity, macrosomia and cesarean delivery. Gestational age-adjusted standard deviation for birth weight was calculated using a China reference chart. SGA and LGA were defined as the gestational age adjusted birth weight less than the 10th percentile and greater than the 90th percentile, respectively. Prematurity was defined as birth at less than 37 weeks of gestation. Macrosomia was defined as neonates with birth weight over 4000 grams.
Comparison of maternal-infants adverse outcomes of this study with other cohorts

Searching pre-pregnancy BMI and maternal-infant adverse outcomes in PubMed, we selected three independent cohorts, normal Chinese women \(^{17}\), Japanese women \(^{18}\), European and North American women \(^{14}\) for comparison analysis. The adverse outcomes in each cohort were compared with women with GDM. The 95%CI of the ORs for adverse outcomes were calculated based on a computational formula. Continuous data were compared using one-sample t-test. The \(p<0.05\) was considered significantly different.

Statistical analysis

Python software (version 3.7.0) was used to process the data. R software (version 3.5.1) was used for data analysis and plotting. Logistic regression analysis in SPSS (version 25.0) was used to assess the by joint effects of maternal pre-pregnancy BMI and GWG on the risks of maternal-infant adverse outcomes.

Ethics Statement

This study was carried out in accordance with the guidelines and approved by the Ethical Committee of Fujian Maternity and Child Health Hospital (Ref.: 2019161). Informed consent was obtained from all the participants.

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Author Contributions

Q.X.Z and H.W.W. contributed to study design, statistical analysis, data interpretation, writing and revising the manuscript. Corresponding authors X.M.J. and H.G.H. contributed to study design, data interpretation and critical revision of the manuscript. Y.L. contributed to data collection and data interpretation. M.P. and L.G. contributed to data interpretation. G.H.L. contributed to statistical analysis, data interpretation and manuscript revision. X.Q.C., J.L.W., X.Y.Z and Y.Q.P. contributed to data collection and data reduction.

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Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
| Variables                        | Underweight group (n=2,031, BMI<18.5) | Normal weight group (n=10,623, 18.5 ≤ BMI<25.0) | Overweight group (n=1,694, 25.0 ≤ BMI<30.0) | Obese group (n=230, BMI ≥30.0) |
|---------------------------------|--------------------------------------|-----------------------------------------------|--------------------------------------------|----------------------------------|
| Age (year)                      | 29.03±4.26                           | 31.21±4.65                                    | 32.25±4.61                                 | 31.04±4.90                      |
| Pre-pregnancy BMI (kg/m²)       | 17.53±0.80                           | 21.40±1.71                                    | 26.67±1.27                                 | 32.10±2.24                      |
| Pre-pregnancy weight (kg)       | 44.98±3.35                           | 54.47±5.44                                    | 67.78±5.38                                 | 81.98±7.74                      |
| BMI before delivery (kg/m²)     | 22.99±1.77                           | 26.54±2.21                                    | 30.82±2.19                                 | 35.63±3.00                      |
| Weight before delivery (kg)     | 58.97±5.43                           | 67.54±6.80                                    | 78.30±7.34                                 | 91.05±9.58                      |
| gestational BMI gain (kg/m²)    | 3.87±2.09                            | 3.68±2.02                                     | 2.91±2.07                                  | 2.56±2.35                       |
| Gestational weeks (week )       | 38.46±2.31                           | 38.43±2.33                                    | 38.36±2.32                                 | 38.45±2.52                      |
| Mode of delivery [NO.(%)]       |                                      |                                               |                                            |                                 |
| Vaginal birth                   | 1528(75.61)                          | 6715(63.21)                                   | 887(52.36)                                 | 101(43.91)                      |
| Cesarean delivery               | 499(24.69)                           | 3876(36.49)                                   | 804(46.46)                                 | 127(55.22)                      |
| Induced labor or Abortion       | 4(0.20)                              | 32(0.30)                                      | 3(0.18)                                    | 2(0.87)                         |
| Type of infant [NO.(%)]         |                                      |                                               |                                            |                                 |
| Classification by gestational age |                                     |                                               |                                            |                                 |
| Premature infant                | 222(10.98)                           | 1207(11.36)                                   | 234(13.81)                                 | 29(12.61)                       |
| Term infant                     | 1805(89.31)                          | 9389(88.38)                                   | 1457(86.00)                                | 199(86.52)                      |
| Classification by birth weight   |                                      |                                               |                                            |                                 |
| Macrosomia                      | 39(1.93)                             | 552(5.20)                                     | 151(8.91)                                  | 30(13.04)                       |
| Classification by the association between gestational age and birth weight |                                      |                                               |                                            |                                 |
| AGA                             | 1728(85.50)                          | 8907(83.85)                                   | 1335(78.81)                                | 166(72.17)                      |
| LGA                             | 80(3.96)                             | 1020(9.60)                                    | 271(16.00)                                 | 53(23.04)                       |
| SGA                             | 214(10.59)                           | 644(6.06)                                     | 82(4.84)                                   | 9(3.91)                         |
| Occupation                      |                                      |                                               |                                            |                                 |
| Self-employed                   | 35(1.72)                             | 244(2.30)                                     | 33(1.95)                                   | 4(1.74)                         |
| Public officer                  | 43(2.12)                             | 238(2.24)                                     | 36(2.13)                                   | 1(0.43)                         |
| Housewife                       | 841(41.41)                           | 4417(41.58)                                   | 729(43.03)                                 | 94(40.87)                       |
| Student                         | 2(0.10)                              | 1(0.01)                                       | 1(0.06)                                    | 0(0.00)                         |
| Medical personnel               | 19(0.94)                             | 96(0.90)                                      | 4(0.24)                                    | 4(1.74)                         |
| Employee                        | 956(47.07)                           | 4856(45.71)                                   | 744(43.92)                                 | 114(49.57)                      |
| Freelance                       | 139(6.84)                            | 771(7.26)                                     | 147(8.68)                                  | 13(5.65)                        |

**Abbreviations:** BMI, body mass index; GWG, Gestational weight gain; AGA, appositeness for gestational age; LGA, large for gestational age; SGA, small for gestational age.
Table 2. Comparisons of the GWG in Chinese women with GDM with the NAM recommendation (n=14,578)

| Pre-pregnant BMI (kg/m²) | GWG (kg) | The GWG range (kg) | The rate of GWG (kg/week) |
|--------------------------|----------|--------------------|--------------------------|
|                          | $\bar{X}$ ±SD | GDM women (minimum-maximum) | The NAM recommended range * | GDM women [Mean(minimum-maximum)] | The NAM recommended range * | t-value | p-value |
| Underweight group        | 14.00±4.06 | 5.95-21.95         | 12.5-18                  | 0.51(0.22-0.80)                | 0.51(0.44-0.58)                | 0.18     | 0.86     |
| Normal weight group      | 13.08±4.47 | 4.23-21.83         | 11.5-16                  | 0.48(0.15-0.80)                | 0.42(0.35-0.50)                | 36.15    | <0.05    |
| Overweight group         | 10.54±4.91 | 0.88-21.12         | 7-11.5                   | 0.39(0.03-0.75)                | 0.28(0.23-0.33)                | 24.15    | <0.05    |
| Obese group              | 9.10±5.54 | -1.76-19.95        | 5-9                      | 0.33(-0.09-0.76)               | 0.22(0.17-0.27)                | 8.24     | <0.05*   |

Abbreviations: BMI, body mass index; GWG, Gestational weight gain; GDM, gestational diabetes mellites.

* The values were recommended by the National Academy of Medicine guidelines in 2009.
Table 3. The risks of maternal or infant adverse outcomes of participants (n=14,578)

| Variables          | n    | LGA (%) | SGA (%) | Prematurity (%) | Macrosomia (%) | Cesarean delivery (%) | Total adverse outcomes (%) |
|--------------------|------|---------|---------|-----------------|----------------|------------------------|---------------------------|
| **Underweight group** |      |         |         |                 |                |                        |                           |
| (Pre-pregnant BMI < 18.5, 12.5kg ≤ Recommended GWG ≤ 18kg) | 2031 | 80(3.94) | 214(10.54) | 217(10.68) | 39(1.92) | 499(24.57) | 1049(51.65) |
| Lower than recommended GWG (GWG < 12.5kg) | 742  | 13(1.75) | 100(13.48) | 114(15.36) | 7(0.94)  | 172(23.18) | 406(54.72)  |
| Equal to recommended GWG (12.5kg ≤ GWG ≤ 18.0kg) | 997  | 42(4.21) | 94(9.42)   | 79(7.92)   | 19(1.91)  | 233(23.37) | 467(46.84)  |
| Higher than recommended GWG (GWG > 18.0kg) | 292  | 25(8.56) | 20(6.85)   | 24(8.22)   | 13(4.45)  | 94(32.19)  | 176(60.27)  |
| **Normal weight group** |      |         |         |                 |                |                        |                           |
| (18.5 ≤ Pre-pregnant BMI < 25.0, 11.5kg ≤ Recommended GWG ≤ 16kg) | 10623 | 1020(9.60) | 644(6.06) | 1182(11.13) | 552(5.20) | 3876(36.49) | 7274(68.47) |
| Lower than recommended GWG (GWG < 11.5kg) | 3894 | 214(5.50) | 273(7.01)  | 527(13.53) | 111(2.85) | 1249(32.07) | 2374(60.97) |
| Equal to recommended GWG (11.5kg ≤ GWG ≤ 16.0kg) | 4303 | 436(10.13) | 253(5.88)  | 397(9.23)  | 223(5.18) | 1579(36.70) | 2888(67.12) |
| Higher than recommended GWG (GWG > 16.0kg) | 2426 | 370(15.25) | 118(4.86)  | 258(10.63) | 218(8.99) | 1048(43.20) | 2012(82.93) |
| **Overweight group** |      |         |         |                 |                |                        |                           |
| (25.0 ≤ Pre-pregnant BMI < 30.0, 7kg ≤ Recommended GWG ≤ 11.5kg) | 1694 | 271(15.98) | 82(4.84)   | 233(13.75) | 151(8.91) | 804(47.46) | 1541(90.97) |
| Lower than recommended GWG (GWG < 7kg) | 396  | 32(8.08)  | 24(6.06)   | 61(15.40)  | 16(4.04)  | 159(40.15) | 292(73.74)  |
| Equal to recommended GWG (7kg ≤ GWG ≤ 11.5kg) | 629  | 88(13.99) | 32(5.09)   | 92(14.63)  | 44(7.00)  | 291(46.26) | 547(86.96)  |
| Higher than recommended GWG (GWG > 11.5kg) | 669  | 151(22.57) | 26(3.89)   | 80(11.96)  | 91(13.60) | 354(52.91) | 702(104.93) |
| **Obese group**     |      |         |         |                 |                |                        |                           |
| (Pre-pregnant BMI ≥ 30.0, 5kg ≤ Recommended GWG ≤ 9kg) | 230  | 53(21.14) | 9(3.91)    | 29(12.61)  | 30(13.04) | 127(55.22) | 248(107.83) |
| Lower than recommended GWG (GWG < 5kg) | 50   | 8(16.00)  | 3(6.00)    | 8(16.00)   | 4(8.00)   | 22(44)     | 45(90.00)   |
| Equal to recommended GWG (5kg ≤ GWG ≤ 9kg) | 72   | 13(18.06) | 6(8.33)    | 11(15.27)  | 7(9.72)   | 41(56.94)  | 78(108.33)  |
| Higher than recommended GWG (GWG > 9kg) | 108  | 32(29.63) | 0          | 10(9.26)   | 19(17.59) | 64(59.26)  | 125(115.74) |

**Abbreviations:** BMI, body mass index; GWG, Gestational weight gain; LGA, large for gestational age; SGA, small for gestational age.
Table 4. The odd ratios (95% confidence intervals) of maternal-infant adverse outcomes by joint effects of maternal pre-pregnancy body mass index and gestational weight gain

| Maternal-infant adverse outcomes | Underweight group (n=2,031, BMI<18.5) | Normal weight group (n=10,623, 18.5≤BMI<25.0) | Overweight group (n=1,694, 25.0≤BMI<30.0) | Obese group (n=230, BMI≥30.0) | p-value |
|---------------------------------|---------------------------------------|---------------------------------------------|------------------------------------------|---------------------------------|---------|
| LGA                             | 0.368 (0.291, 0.466)                  | 2.272 (1.952, 2.646)                       | 4.364 (3.132, 6.081)                     | p<0.001                         |         |
| Below                           | 0.419 (0.223, 0.787)                  | 0.706 (0.561, 0.889)                       | 0.882 (0.538, 1.446)                     | 1.055(0.364, 3.063)             |         |
| Within                          | 1                                     | 1                                           | 1                                        | 1                               |         |
| Above                           | 1.992 (1.187, 3.342)                  | 1.050 (0.832, 1.325)                       | 0.935 (0.604, 1.448)                     | 1.394(0.518, 3.746)             |         |
| p-value                         | p=0.453                               | p<0.001                                    | p=0.011                                  | p=0.085                         |         |
| SGA                             | 1.899(1.605, 2.246)                   | 1                                           | 0.716 (0.562, 0.913)                     | 0.549 (0.279, 1.082)            | p<0.001 |
| Below                           | 1.103 (0.682, 1.783)                  | 1.031 (0.787, 1.351)                       | 1.131 (0.538, 2.377)                     | 1.843(0.156, 21.829)            |         |
| Within                          | 1                                     | 1                                           | 1                                        | 1                               |         |
| Above                           | 1.042 (0.534, 2.031)                  | 0.996 (0.731, 1.357)                       | 0.892 (0.402, 1.978)                     | 0.00                            |         |
| p-value                         | p<0.001                               | p<0.001                                    | p=0.419                                  | p=0.060                         |         |
| Prematurity                     | 0.956                                 | 1                                           | 0.997                                    | 1.175                           | p=1.00  |
| Below                           | 1.045                                 | 0.940                                       | 0.821                                    | 0.055                           |         |
| Within                          | 1                                     | 1                                           | 1                                        | 1                               |         |
| Above                           | 1.120                                 | 1.139                                       | 0.976                                    | 9.848                           |         |
| p-value                         | p=1.00                                | p=1.00                                      | p=1.00                                   | p=1.00                          |         |
| Macrosomia                      | 0.322 (0.231, 0.447)                  | 1                                           | 2.365 (1.943, 2.878)                     | 4.761 (3.164, 7.163)            | p<0.001 |
| Below                           | 1.364 (0.435, 4.277)                  | 0.930 (0.688, 1.257)                       | 1.178(0.616, 2.254)                      | 0.648(0.182, 2.313)             |         |
| Within                          | 1                                     | 1                                           | 1                                        | 1                               |         |
| Above                           | 0.640 (0.185, 2.216)                  | 1.010 (0.746, 1.368)                       | 0.756(0.431, 1.326)                      | 1.738(0.708, 4.267)             |         |
| p-value                         | p=0.059                               | p<0.001                                    | p=0.002                                  | p=0.321                         |         |
| Cesarean delivery              | 0.528 (0.420, 0.664)                  | 1                                           | 1.744 (1.488, 2.044)                     | 2.412 (1.648, 3.532)            | p<0.001 |
| Below                           | 0.845 (0.506, 1.409)                  | 0.931 (0.742, 1.168)                       | 1.074(0.663, 1.740)                      | 0.621(0.223, 1.731)             |         |
| Within                          | 1                                     | 1                                           | 1                                        | 1                               |         |
| Above                           | 2.205 (1.256, 3.873)                  | 1.210 (0.946, 1.548)                       | 1.123(0.703, 1.794)                      | 0.662(0.284, 1.546)             |         |
| p-value                         | p=0.043                               | p<0.001                                    | p=0.092                                  | p=0.563                         |         |
| Total adverse outcomes          | 0.780(0.691, 0.880)                   | 1                                           | 1.742 (1.546, 1.962)                     | 2.489 (1.857, 3.335)            | p<0.001 |
| Below                           | 1.014 (0.696, 1.476)                  | 0.934 (0.801, 1.090)                       | 1.092(0.761, 1.568)                      | 0.944(0.371, 2.404)             |         |
| Within                          | 1                                     | 1                                           | 1                                        | 1                               |         |
| Above                           | 1.896 (1.170, 3.074)                  | 1.170 (0.988, 1.386)                       | 1.086(0.756, 1.559)                      | 0.645(0.258, 1.612)             |         |
| p-value                         | p=0.019                               | p<0.001                                    | p=0.079                                  | p=0.995                         |         |

Abbreviations: BMI, body mass index; GWG, Gestational weight gain.
**Figure 1.** The GWG trajectory among Chinese women with GDM. (a-d) The GWG trajectory from 12\textsuperscript{th} gestational week to 40\textsuperscript{th} gestational week in underweight, normal weight, overweight and obesity group were shown, respectively.

**Figure 2.** The risk heat map of the maternal-infant adverse outcomes. (a) Values represented the risks of any maternal-infant adverse outcomes. (b) The percentages of participants for each combination of BMI and GWG.

**Figure 3.** The risks of the maternal-infant adverse outcomes in four pre-pregnancy BMI subgroups. (a-d) The risks for adverse maternal-infant outcomes in underweight, normal weight, overweight and obesity group were demonstrated respectively. LGA: large for gestational age; SGA: small for gestational age.

**Figure 4.** Meta-analysis of the associations of maternal-infant adverse outcomes with pre-pregnancy BMI in three independent cohorts. (a) Forest plot showed the different adverse outcomes between women with GDM and normal Chinese women in four pre-pregnancy BMI subgroups. (b) The different adverse outcomes between women with GDM and Japanese women in four pre-pregnancy BMI subgroups were compared. (c) Compared with Chinese GDM women, the incidences of adverse outcomes in European and North American women were tested.
Figure 1.

(a) Underweight

(b) Normal weight

(c) Overweight

(d) Obese
Figure 2.

Any maternal-infant adverse outcome (%):

Participants (%):

The gestational weight gain (kg)

Pre-pregnancy BMI (kg/cm^2)

Participants (‰):

Figur2.

Particpants (‰):
Figure 3.

a) Underweight group

b) Normal weight group

c) Overweight group

d) Obese group

Graphs showing the risk of maternal-infant adverse outcomes for different weight groups based on total gestational weight gain, kg.
### Figure 4.

| Outcomes                | GDM women | Chinese | OR(95% CI) | Japanese | OR(95% CI) | European and North American | OR(95% CI) |
|-------------------------|-----------|---------|------------|----------|------------|----------------------------|------------|
| **Underweight group**   |           |         |            |          |            |                            |            |
| large for gestational age | 0.04      | 0.04    | 0.99(0.98, 1.00) | 0.06    | 0.7(0.42, 1.00) | 0.03                       | 1.21(1.05, 1.37) |
| small for gestational age | 0.12      | 0.18    | 0.64(0.27, 1.02) | 0.15    | 0.77(0.56, 0.99) | 0.21                       | 0.67(0.09, 1.05) |
| Prematurity             | 0.12      | 0.03    | 4.48(2.31, 5.76) | 0.14    | 0.86(0.74, 0.99) | 0.05                       | 2.32(1.60, 3.04) |
| Macrosomia              | 0.02      | 0.04    | 0.47(0.17, 1.11) | 0       | 7.36(5.66, 9.06) | 0.13                       | 2.42(1.67, 3.17) |
| Cesarean delivery       | 0.33      | 1.23    | 0.27(0.86, 1.39) | 0.29    | 1.12(1.02, 1.22) | 0.13                       | 0.65(0.29, 1.45) |
| **Normal weight group** |           |         |            |          |            |                            |            |
| large for gestational age | 0.11      | 0.1     | 1.06(1.01, 1.11) | 0.11    | 0.95(0.91, 0.99) | 0.09                       | 1.21(1.05, 1.37) |
| small for gestational age | 0.06      | 0.1     | 0.65(0.27, 1.02) | 0.09    | 0.68(0.35, 1.01) | 0.11                       | 0.57(0.10, 1.05) |
| Prematurity             | 0.13      | 0.03    | 4.19(2.97, 5.41) | 0.11    | 1.10(1.02, 1.18) | 0.04                       | 3.03(2.08, 3.97) |
| Macrosomia              | 0.05      | 0.09    | 0.58(0.12, 1.04) | 0.01    | 7.94(1.18, 9.70) | 0.15                       | 3.74(2.62, 4.86) |
| Cesarean delivery       | 0.57      | 1.71    | 0.34(0.59, 1.26) | 0.37    | 1.56(1.18, 1.93) | 0.15                       | 4.15(2.94, 5.36) |
| **Overweight group**    |           |         |            |          |            |                            |            |
| large for gestational age | 0.19      | 0.18    | 1.09(1.02, 1.16) | 0.21    | 0.91(0.82, 0.99) | 0.15                       | 1.26(1.06, 1.46) |
| small for gestational age | 0.05      | 0.07    | 0.69(0.37, 1.01) | 0.08    | 0.65(0.29, 1.02) | 0.08                       | 0.62(0.20, 1.03) |
| Prematurity             | 0.16      | 0.04    | 4.54(3.25, 5.82) | 0.13    | 1.21(1.05, 1.37) | 0.04                       | 3.56(2.48, 4.64) |
| Macrosomia              | 0.1       | 0.16    | 0.60(1.64, 1.04) | 0.02    | 5.46(4.02, 6.91) | 0.15                       | 1.4(1.11, 1.69)  |
| Cesarean delivery       | 0.9       | 3.05    | 0.3(0.74, 1.33)  | 0.58    | 1.55(1.18, 1.93) | 0.22                       | 4.15(2.94, 5.36) |
| **Obese group**         |           |         |            |          |            |                            |            |
| large for gestational age | 0.3       | 0.29    | 1.03(1.00, 1.05) | 0.29    | 1.03(1.00, 1.05) | 0.21                       | 1.4(1.11, 1.69)  |
| small for gestational age | 0.04      | 0.06    | 0.67(0.34, 1.01) | 0.08    | 0.54(0.01, 1.07) | 0.08                       | 0.51(0.07, 1.08) |
| Prematurity             | 0.14      | 0.05    | 2.79(1.92, 3.67) | 0.14    | 1.05(1.01, 1.10) | 0.06                       | 2.49(1.71, 3.27) |
| Macrosomia              | 0.15      | 0.25    | 0.60(0.17, 1.03) | 0.03    | 4.74(3.42, 6.07) | 0.31                       | 3.94(2.77, 5.11) |
| Cesarean delivery       | 1.23      | 5.1     | 0.24(0.97, 1.45) | 0.75    | 1.64(1.22, 2.06) | 0.31                       | 3.74(2.62, 4.86) |

The estimates are represented in a graph format with the x-axis indicating the estimates and the y-axis showing the outcomes. The OR(95% CI) values are depicted alongside the estimates, with different colors and markers to distinguish between the groups and outcomes.