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RESEARCH ARTICLE

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# Patterns of maternal gestational weight gain in association with allergic diseases in offspring: A prospective cohort study

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**Abstract**

**Objective:** To evaluate the association between patterns of gestational weight gain (GWG) and allergic diseases in offspring.

**Design:** Prospective cohort study.

**Setting:** Prenatal clinics in Wuhan, China.

**Population:** A cohort of 2546 mother and offspring pairs were enrolled before 16 weeks of gestation and followed up to 24 months postpartum.

**Methods:** Maternal body weights were measured regularly during pregnancy, and their GWG patterns were estimated using the growth mixture model. Robust Poisson models were used to evaluate relative risk (RR) and 95% CI after multivariable adjustment.

**Main outcome measures:** Offspring atopic allergy and allergic contact dermatitis were defined according to a physician's diagnosis reported by the mother, and food allergy was reported by the mother.

**Results:** Three GWG patterns were identified: 18.1% (461) of the women were described as pattern 1, characterised by rapid GWG earlier in pregnancy; 56.6% (1442) of the women were described as pattern 2, with steady GWG throughout pregnancy; and 25.3% (643) of the women was described as pattern 3, with rapid GWG later in pregnancy. By the age of 24 months, 360 (14.1%), 109 (4.3%) and 757 (29.7%) offspring had atopic allergy, allergic contact dermatitis or food allergy, respectively. Compared with women in GWG pattern 2, the RRs (95% CIs) among women in pattern 1 were 0.74 (0.55–0.99) for atopic allergy, 0.64 (0.36–1.15) for allergic contact dermatitis and 0.95 (0.81–1.12) for food allergy.

**Conclusions:** Maternal GWG pattern characterised by rapid GWG earlier in pregnancy was associated with a lower risk of atopic allergy in offspring.

KEYWORDS
allergic disease, asthma, dermatitis, diabetes, food allergy, gestational weight gain, nutrition, overweight, pattern, pregnancy, underweight

## 1 | INTRODUCTION

Globally, the prevalence of allergic diseases is increasing.[1] It is estimated that 2–4 billion people will suffer from allergic diseases, such as asthma, allergic rhinitis and atopic dermatitis, by 2050 and have their health-related quality of life impaired.[2,3] Prior studies have explored a range of genetic and environmental factors that may affect the development of allergic diseases, some of which have focused on prenatal factors, hypothesising that these factors may affect offspring allergic disease by changing the intrauterine environment.[4] Several studies have indicated an association between maternal pre-pregnancy obesity and allergic diseases in offspring.[5–7] However, the influence of maternal gestational

weight gain (GWG) on allergic diseases in offspring remains less well understood.

Although some studies have suggested an association between extremely low or high total GWG and allergic diseases in offspring,[8–13] defined as the difference between the last measurement of maternal weight before delivery and pre-pregnancy body weight, the total GWG cannot capture longitudinal changes in maternal weight throughout pregnancy. Moreover, evidence has indicated that GWG in the first trimester primarily contributes to maternal fat gain, whereas GWG in the second and third trimesters primarily contributes to fetal and placental growth.[14,15] Investigating maternal GWG patterns during pregnancy will enable us to understand the association between maternal weight change during pregnancy and offspring allergic diseases more comprehensively.

Growth mixture models use a latent approach to identify group-based heterogeneous development trajectories over time.[16] Using longitudinal weight gain data during pregnancy in a prospective cohort, the current study aimed to identify different maternal GWG trajectories across pregnancy by using the growth mixture model and to evaluate whether these GWG patterns are associated with atopic allergy, allergic contact dermatitis and food allergy in offspring.

## 2 | METHODS

### 2.1 | Study population

The Tongji Maternal and Child Health Cohort (TMCHC) is a continuing prospective cohort study in Wuhan, China, aiming to evaluate the associations of maternal nutrition, lifestyle and environmental factors during pregnancy with health outcomes of the mother and child pairs. Pregnant women who attended prenatal care before 16 weeks of gestation were recruited from January 2013 to May 2016 and were followed up regularly.[17]

This study was performed in accordance with the Helsinki declaration. The study was approved by the ethics review committee of Tongji Medical College of Huazhong University of Science and Technology (no. 201302), and all participants provided written informed consent upon enrolment.

A total of 3128 mothers with a singleton live birth were followed up until 24 months postpartum. After excluding mothers with pre-existing diabetes ($n$ = 3), chronic hypertension ($n$ = 5), severe autoimmune diseases ($n$ = 3), no more than two weight measurements during pregnancy ($n$ = 466) or preterm birth ($n$ = 105), 2546 mother–offspring pairs were included in the current study.

### 2.2 | Gestational weight gain

Maternal self-reported pre-pregnancy weight was recorded at enrolment, and their current weight and height wearing light clothing and no shoes was measured by trained nurses. Maternal weight was measured in the same way at each following antenatal visit during pregnancy.

Gestational weight gain up to a specific gestational week was calculated by subtracting the pre-pregnancy weight from the current weight, and then this value was used to fit GWG patterns with the growth mixture model. In addition, total GWG was defined as the difference between the last measured weight before delivery and the pre-pregnancy weight, categorised as inadequate, adequate and excessive, according to the recommendations of the National Academy of Medicine (NAM; formerly the Institute of Medicine, IOM).[18] Weekly GWG in the first, second and third trimesters was defined as the difference between the mean weight at 11–14 weeks of gestation and the pre-pregnancy weight, the difference between the mean weight at 24–28 weeks of gestation and the mean weight at 11–14 weeks of gestation, and the difference between the last measured weight before delivery and the mean weight at 24–28 weeks of gestation, divided by the weeks between, respectively.

### 2.3 | Allergic disease

The information on allergic diseases in offspring was reported by their mothers based on medical record through telephone interviews at 3, 6, 12 and 24 months postpartum. Mothers were asked, 'Has your child seen a physician because of any allergic disease since the last assessment?'. If the mother answered 'yes', the diagnosis and number of each allergic disease episodes were recorded. Asthma, eczema, allergic rhinitis and allergic contact dermatitis were defined based on the reported diagnosis. According to the International Classification of Diseases, 11th Revision (ICD-11) published by the World Health Orgnization,[19] we further defined physician-diagnosed asthma, eczema and allergic rhinitis as atopic allergy. Food allergy in offspring was reported by their mothers at 6, 12 and 24 months postpartum. Mothers were asked, 'Has your child ever had a food allergy until now?'. If the answer was 'yes', the type of food allergy and the age (in months) of onset were recorded.

### 2.4 | Covariates

Maternal baseline characteristics were obtained by face-to-face questionnaires at enrolment, including maternal age, ethnicity (Han Chinese or other), parity (primiparous or multiparous), education level (<16 or ≥16 years), average personal income (<5000 or ≥5000 Chinese Yuan), pre-pregnancy insomnia (sometimes, seldom or never), smoking in early pregnancy (both active and passive smoking, yes or no) and maternal allergy history (yes or no). Maternal pre-pregnancy body mass index (BMI) was calculated as self-reported pre-pregnancy weight (kg) divided by the square of the measured height ($m^2$), categorised as underweight (<18.5 kg/$m^2$), normal weight (18.5–23.9 kg/$m^2$) and overweight/obese (≥24.0 kg/$m^2$), according to Chinese guidelines.[20]

Information on birth outcomes was acquired from hospital records, including the date of delivery, mode of delivery (caesarean or vaginal delivery), sex of offspring, and birthweight and length. Information on feeding status was obtained by telephone interview based on questionnaires at the offspring ages of 3, 6, 12 and 24 months, including the practice of breastfeeding and bottle feeding.

## 2.5 | Statistical analyses

Based on GWG up to specific gestational weeks, GWG patterns were estimated by using the growth mixture model, a latent approach to identify clusters of participants with similar trajectories over time.[16] Pregnant women were distributed into multiple heterogeneous GWG trajectories across pregnancy, and those with the similar pattern of GWG were assigned to the same group. The longitudinal models were fitted with linear, quadratic and cubic terms for gestational weeks, and the optimal numbers of classes was determined according to Bayesian information criteria. A posterior probability assigned to each latent class was calculated for each participant by the growth mixture model, and each participant was assigned to the class with the highest probability. Considering the clinical implications of the classes, we imposed the following conditions: (1) each class included at least 5% of participants; and (2) the mean posterior probability of each class was higher than 75%.[21]

We performed robust Poisson regression models to estimate the relative risk (RR) and 95% CI for the risk of atopic allergy, allergic contact dermatitis and food allergy. To evaluate whether the association of GWG patterns with allergic diseases was confounded by maternal characteristics and lifestyle factors, multivariable models were conducted to adjust for maternal age (years), parity (primiparous or multiparous), education level (<16 or ≥16 years), average personal income (<5000 or ≥5000 Chinese Yuan), smoking in early pregnancy (yes or no), maternal allergy history (yes or no), insomnia (sometimes, seldom or never) and pre-pregnancy BMI (<18.5, 18.5–24.0 or ≥24.0 kg/m$^2$). As seasonal lifestyle factors may affect a pregnant woman's body weight, and the season of delivery has been reported to be associated with allergic diseases in offspring,[22] the season of delivery (spring, summer, autumn or winter) was further adjusted to test the robustness of the associations. We imputed missing values on maternal education level (2.7%) and average personal income (1.7%) using multiple imputation ($m$ = 5 imputations) with chained equations.[23]

In the sensitivity analyses we excluded pregnant women with GWGs of <5 kg or ≥20 kg because prior studies have indicated an association of extremely low or high GWG with allergic diseases in offspring.[9–12] Also, we repeated the analyses among mothers without a history of allergy to test the robustness of the association in low-risk populations, as maternal allergy history is a known risk factor for allergic diseases in offspring.[24] Additionally, to validate the association of GWG patterns identified by the growth mixture model, we also grouped participants according to their trimester-specific GWG and evaluated their association with the outcomes.

To evaluate the consistency of the association between GWG patterns and allergic diseases in all maternal BMI, season of delivery and offspring sex subgroups, stratified analyses were performed by these factors and the interactions were tested with the likelihood ratio test.

A two-sided $p < 0.05$ was considered statistically significant for all tests. All analyses were conducted using R 3.6.1 (The R Foundation, www.r-project.org), with the package lcmm, and STATA 16 (StataCorp, College Station, Texas, USA).

# 3 | RESULTS

Among the 2546 pregnant women, the mean (SD) values were 20.9 kg/m$^2$ (2.7 kg/m$^2$) for pre-pregnancy BMI, 28.3 years (3.5 years) for age and 15.9 kg (4.5 kg) for total GWG (Table 1). The records indicate that 13.2%, 39.4% and 47.5% of them had inadequate, adequate and excessive total GWG, respectively. By the age of 24 months, 360 (14.1%) offspring had atopic allergy, 109 (4.3%) had allergic contact dermatitis and 757 (29.7%) had food allergy, mainly with allergies to eggs, fish, shrimp and other seafoods (Table S1).

The whole number of weight measurements was 25 540, with a median of 11 measurements (interquartile range, IQR 8–12), ranging from three to 18 measurements per woman. The mean gestations at the first and last weight measurements were 12.6 weeks (SD 1.44 weeks) and 38.1 weeks (SD 1.95 weeks), respectively. The results of growth mixture models, presented in Tables S2 and S3, showed that the inclusion of a cubic term improved the model fit. Of the models with a cubic term, the model with three GWG patterns was identified (Figure 1). A total of 461 (18.1%) pregnant women were identified as following pattern 1, characterised by rapid GWG earlier in pregnancy (median weekly GWGs of the first, second and third trimester: 0.15, 0.68 and 0.39 kg/week); 1442 (56.6%) pregnant women were identified as following pattern 2, characterised by steady GWG in pregnancy (median weekly GWGs of the first, second and third trimester: 0.08, 0.55 and 0.54 kg/week); and 643 (25.3%) pregnant women were identified as following pattern 3, characterised by rapid GWG later in pregnancy (median weekly GWGs of the first, second and third trimester: 0.03, 0.49 and 0.78 kg/week) (Table S4). Pattern 2 was designated as the reference group, as the GWG of this pattern was close to the reference curve of the INTERGROWTH-21st Project.[25]

Mothers with pattern 1 were slightly older and more likely to give birth in spring and summer; mothers with pattern 3 were slightly younger, less likely to be underweight before pregnancy, more likely to give birth in autumn and winter, and had a greater total GWG. There were no significant differences in total GWG between mothers with patterns 1 and 2 (Table 1).

In addition, to validate the results of the GWG patterns identified by the growth mixture model, participants were

**TABLE 1** Characteristics of the study population according to pattern of gestational weight gain (GWG).

| Characteristics | GWG patterns | | | | |
|---|---|---|---|---|---|
| | Total ($n$ = 2546) | Pattern 1 ($n$ = 461) | Pattern 2 ($n$ = 1442) | Pattern 3 ($n$ = 643) | $p$ |
| Pre-pregnancy BMI, mean (SD), kg/m$^2$ | 20.9 (2.7) | 21.1 (2.7) | 20.7 (2.7) | 21.1 (2.6) | 0.001 |
| Pre-pregnancy BMI, $n$ (%) | | | | | |
| <18.5 kg/m$^2$ | 475 (18.7) | 73 (15.8) | 318 (22.1) | 84 (13.1) | <0.001 |
| 18.5–23.9 kg/m$^2$ | 1749 (68.7) | 314 (68.1) | 963 (66.8) | 472 (73.4) | |
| ≥24.0 kg/m$^2$ | 322 (12.7) | 74 (16.1) | 161 (11.2) | 87 (13.5) | |
| Height, mean (SD), cm | 160.2 (5.0) | 160.1 (4.9) | 160.0 (5.0) | 160.2 (4.9) | 0.938 |
| Maternal age, mean (SD), years | 28.3 (3.5) | 28.9 (3.4) | 28.5 (3.5) | 27.6 (3.4) | <0.001 |
| Maternal education, $n$ (%) | | | | | |
| <16 years | 980 (38.5) | 165 (35.8) | 522 (36.2) | 293 (45.6) | <0.001 |
| ≥16 years | 1498 (58.8) | 287 (62.3) | 882 (61.2) | 329 (51.2) | |
| Missing | 68 (2.7) | 9 (2.0) | 38 (2.6) | 21 (3.3) | |
| Average personal income, $n$ (%) | | | | | |
| <5000 ¥[a] | 912 (35.8) | 164 (35.6) | 509 (35.3) | 239 (37.2) | 0.507 |
| ≥5000 ¥ | 1590 (62.5) | 293 (63.6) | 906 (62.8) | 391 (60.8) | |
| Missing | 44 (1.7) | 4 (0.9) | 27 (1.9) | 13 (2.0) | |
| Ethnicity (Han Chinese), $n$ (%) | 2485 (97.6) | 448 (97.2) | 1408 (97.6) | 629 (97.8) | 0.781 |
| Primiparous, $n$ (%) | 2126 (83.5) | 391 (84.8) | 1184 (82.1) | 551 (85.7) | 0.088 |
| Insomnia before pregnancy, $n$ (%) | | | | | |
| Sometimes | 276 (10.8) | 54 (11.7) | 153 (10.6) | 69 (10.7) | 0.919 |
| Seldom | 791 (31.1) | 139 (30.2) | 457 (31.7) | 195 (30.3) | |
| Never | 1479 (58.1) | 268 (58.1) | 832 (57.7) | 379 (58.9) | |
| Smoking in early pregnancy, $n$ (%) | 208 (8.2) | 39 (8.5) | 119 (8.3) | 50 (7.8) | 0.906 |
| Maternal history of allergy, $n$ (%) | 239 (9.4) | 56 (12.2) | 128 (8.9) | 55 (8.6) | 0.078 |
| Gestational age at delivery, mean (SD), weeks | 39.6 (1.1) | 39.6 (1.1) | 39.6 (1.1) | 39.7 (1.1) | 0.112 |
| Total GWG, mean (SD), kg | 15.9 (4.5) | 15.7 (4.6) | 15.5 (4.1) | 17.0 (5.0) | <0.001 |
| Season of delivery, $n$ (%) | | | | | |
| Spring (Mar–May) | 560 (22.0) | 176 (38.2) | 307 (21.3) | 77 (12.0) | <0.001 |
| Summer (Jun–Aug) | 666 (26.2) | 151 (32.8) | 405 (28.1) | 110 (17.1) | |
| Autumn (Sep–Nov) | 886 (34.8) | 82 (17.8) | 513 (35.6) | 291 (45.3) | |
| Winter (Dec–Feb) | 434 (17.1) | 52 (11.3) | 217 (15.1) | 165 (25.7) | |
| Caesarean section, $n$ (%) | 1056 (41.5) | 194 (42.1) | 604 (41.9) | 258 (40.1) | 0.721 |
| Male offspring, $n$ (%) | 1381 (54.2) | 245 (53.2) | 798 (55.3) | 338 (52.6) | 0.438 |
| Birthweight, mean (SD), g | 3371 (402) | 3436 (396) | 3373 (395) | 3323 (415) | <0.001 |
| Breastfeeding duration, mean (SD), mon | 10.5 (5.8) | 10.7 (6.0) | 10.6 (5.8) | 10.0 (5.8) | 0.082 |

Abbreviations: BMI, body mass index; GWG, gestational weight gain.

[a]¥, Chinese Yuan; ¥1 ≈ $0.16.

further categorised according to their weekly GWG in the following two periods: the first two trimesters and the third trimester, where weekly GWG in the first two trimesters was calculated as the difference between the mean weight at 24–28 weeks of gestation and the pre-pregnancy weight divided by the weeks between. Women were categorised into Q1, Q2&3 and Q4 based on quartiles of weekly GWG in each period, according to pre-pregnancy BMI group, and then the following groups with similar patterns to the growth mixture model-based GWG patterns were selected: Q4–Q1 and Q4–Q2&3 (similar to pattern 1); Q2&3–Q2&3 (similar to pattern 2); and Q2&3–Q4 and Q1–Q4 (similar to pattern 3) (Table S5).

Associations of GWG patterns with offspring allergic diseases were presented in Table 2. Compared with mothers following GWG pattern 2, the RRs (95% CIs) among mothers

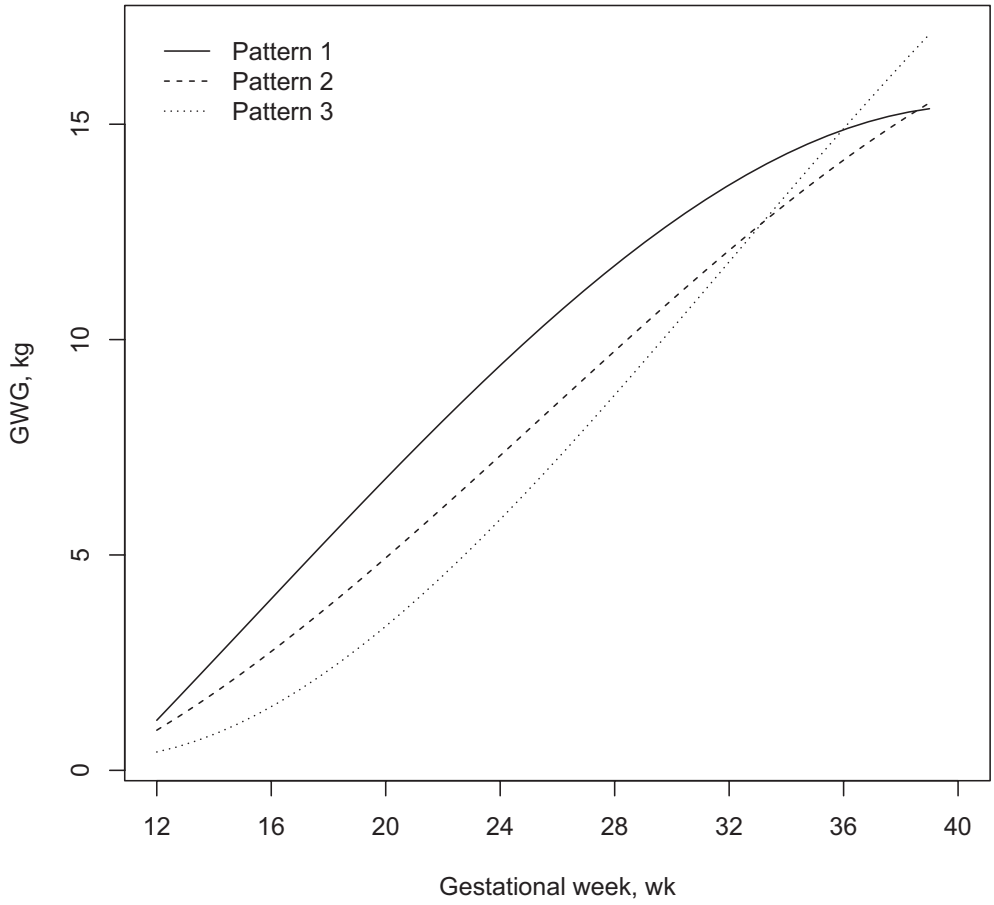


**FIGURE 1** Patterns of gestational weight gain (GWG) in the study population identified by the growth mixture model.

following pattern 1 were 0.64 (0.48–0.86) for atopic allergy, 0.66 (0.37–1.16) for allergic contact dermatitis and 0.94 (0.80–1.11) for food allergy, after adjustment for maternal age, parity, education level, average personal income, smoking in early pregnancy, maternal allergic history, insomnia and pre-pregnancy BMI. Among mothers following GWG pattern 3, the RRs (95% CIs) were 0.96 (0.77–1.21) for atopic allergy, 0.99 (0.64–1.55) for allergic contact dermatitis and 0.88 (0.75–1.02) for food allergy. With additional adjustment for season of delivery, the RRs (95% CIs) among pregnant women following pattern 1 were 0.74 (0.55–0.99) for atopic allergy, 0.64 (0.36–1.15) for allergic contact dermatitis and 0.95 (0.81–1.12) for food allergy.

In sensitivity analyses, similar results were found among women with total GWGs of 5–20 kg (Table S6) and among women without a history of allergy (Table S7). Additionally, when pregnant women were further grouped according to weekly GWG in the first two trimesters and the third trimester, the Q4–Q1 group was associated with a lower risk of atopic allergy in offspring. Specifically, compared with the Q2&3–Q2&3 group, the RRs (95% CIs) of atopic allergy were 0.54 (0.30–0.97) for the Q4–Q1 group, 0.73 (0.50–1.08) for the Q4–Q2&3 group, 0.85 (0.60, 1.22) for the Q2&3–Q4 group and 0.86 (0.54–1.35) for the Q1–Q4 group, after adjustment for season of delivery and the other covariates mentioned above (Table 3).

Consistent associations of GWG pattern 1 with atopic allergy were found when stratified by maternal pre-pregnancy BMI, season of delivery or offspring sex (all $p > 0.05$ for interaction), especially in those with a pre-pregnancy BMI of <18.5 kg/m$^2$ (RR 0.36, 95% CI 0.14–0.94) or who gave birth in winter or spring (RR 0.43, 95% CI 0.26–0.72) (Table S8).

## 4 | DISCUSSION

### 4.1 | Main findings

In this large prospective cohort study, maternal GWG pattern characterised by rapid GWG earlier in pregnancy was associated with a lower risk of atopic allergy in offspring, whereas there were no associations of GWG patterns with allergic contact dermatitis and food allergy in offspring.

### 4.2 | Strengths and limitations

The current study had some strengths. It was embedded in a large prospective cohort with accurate and repeated weight measurements during pregnancy and detailed information on potential confounding factors. In addition, as the total GWG and GWG patterns reflect two different characteristics

of GWG, the current study took total GWG into account when evaluating the association of GWG patterns with the outcomes.

**TABLE 2** Relative risks (95% CIs) of offspring allergic diseases according to pattern of gestational weight gain (GWG).

| | GWG pattern | | |
|---|---|---|---|
| | **Pattern 1** | **Pattern 2** | **Pattern 3** |
| Atopic allergy | | | |
| Case (%) | 47 (10.2) | 222 (15.4) | 91 (14.2) |
| Model 1 | **0.66 (0.49–0.89)** | Ref. (1.00) | 0.92 (0.73–1.15) |
| Model 2 | **0.64 (0.48–0.86)** | Ref. (1.00) | 0.96 (0.77–1.21) |
| Model 3 | **0.74 (0.55–0.99)** | Ref. (1.00) | 0.87 (0.69–1.09) |
| Allergic contact dermatitis | | | |
| Case (%) | 14 (3.0) | 66 (4.6) | 29 (4.5) |
| Model 1 | 0.66 (0.38–1.17) | Ref. (1.00) | 0.99 (0.64–1.51) |
| Model 2 | 0.66 (0.37–1.16) | Ref. (1.00) | 0.99 (0.64–1.55) |
| Model 3 | 0.64 (0.36–1.15) | Ref. (1.00) | 1.03 (0.66–1.61) |
| Food allergy | | | |
| Case (%) | 137 (29.7) | 444 (30.8) | 176 (27.4) |
| Model 1 | 0.96 (0.82–1.13) | Ref. (1.00) | 0.89 (0.77–1.03) |
| Model 2 | 0.94 (0.80–1.11) | Ref. (1.00) | 0.88 (0.75–1.02) |
| Model 3 | 0.95 (0.81–1.12) | Ref. (1.00) | 0.86 (0.74–1.00) |

*Note*: Model 1 was the crude model. Model 2 was adjusted for maternal age, parity, education level, average personal income, smoking in early pregnancy, maternal allergic history, insomnia and pre-pregnancy BMI. Model 3 was additionally adjusted for season of delivery. Bold values denote statistical significance at the $p < 0.05$ level.

Abbreviations: BMI, body mass index; GWG, gestational weight gain.

The current study also had some limitations. Maternal pre-pregnancy weight was self-reported, which might introduce bias. However, the difference between reported and measured pre-pregnancy weight was small,[26] and the pre-pregnancy weight used in the current study was collected in early pregnancy when the body weight did not significantly change and the recall period was short. Moreover, the definition of allergic diseases was based on the mother's reports of physician-diagnosed diseases, which might lead to an underestimation and misclassification, but these biases were likely to be non-differential and shifted the association towards the null. Furthermore, as most pregnant women were Han Chinese, whether the findings are applicable to pregnant women of other ethnicities deserves further investigation. Additionally, because of the observational design, the associations may subject to residual and unmeasured confounding.

## 4.3 | Interpretation

To the best of our knowledge, this is the first study to evaluate the association of maternal GWG patterns with allergic diseases in offspring. A previous study showed that maternal GWG pattern with rapid GWG earlier in pregnancy was associated with improved birth outcomes among multiparous women,[27] and the current study added that this GWG pattern was associated with a lower risk of atopic allergy in offspring up to 24 months. In the current study, pregnant women of this GWG pattern had higher GWG during the first two trimesters but lower GWG in the third

**TABLE 3** Relative risks (95% CIs) of offspring allergic diseases according to GWG group.

| | Weekly GWG in the first two trimesters and the third trimester | | | | |
|---|---|---|---|---|---|
| | **Q4–Q1** | **Q4–Q2&3** | **Q2&3–Q2&3** | **Q2&3–Q4** | **Q1–Q4** |
| Atopic allergy | | | | | |
| Case (%) | 11 (7.8) | 29 (11.2) | 93 (16.0) | 35 (13.4) | 20 (14.4) |
| Model 1 | **0.49 (0.27–0.89)** | 0.70 (0.47–1.03) | Ref (1.00) | 0.84 (0.58–1.20) | 0.90 (0.58–1.40) |
| Model 2 | **0.46 (0.26–0.83)** | 0.71 (0.48–1.04) | Ref (1.00) | 0.90 (0.63–1.29) | 0.98 (0.63–1.54) |
| Model 3 | **0.54 (0.30–0.97)** | 0.73 (0.50–1.08) | Ref (1.00) | 0.85 (0.60–1.22) | 0.86 (0.54–1.35) |
| Allergic contact dermatitis | | | | | |
| Case (%) | 8 (5.7) | 13 (5.0) | 22 (3.8) | 7 (2.7) | 5 (3.6) |
| Model 1 | 1.50 (0.68–3.30) | 1.33 (0.68–2.59) | Ref (1.00) | 0.71 (0.31–1.64) | 0.95 (0.37–2.47) |
| Model 2 | 1.58 (0.73–3.41) | 1.35 (0.70–2.61) | Ref (1.00) | 0.73 (0.31–1.70) | 0.96 (0.36–2.60) |
| Model 3 | 1.50 (0.69–3.27) | 1.34 (0.69–2.62) | Ref (1.00) | 0.74 (0.32–1.73) | 1.02 (0.37–2.78) |
| Food allergy | | | | | |
| Case (%) | 42 (29.8) | 86 (33.2) | 154 (26.5) | 75 (28.7) | 43 (30.9) |
| Model 1 | 1.10 (0.82–1.48) | **1.25 (1.01–1.56)** | Ref (1.00) | 1.08 (0.85–1.36) | 1.18 (0.89–1.56) |
| Model 2 | 1.10 (0.82–1.47) | 1.23 (0.99–1.53) | Ref (1.00) | 1.06 (0.84–1.35) | 1.15 (0.87–1.54) |
| Model 3 | 1.11 (0.82–1.49) | 1.24 (0.99–1.54) | Ref (1.00) | 1.05 (0.83–1.34) | 1.14 (0.85–1.53) |

*Note*: Model 1 was the crude model. Model 2 was adjusted for maternal age, parity, education level, average personal income, smoking in early pregnancy, maternal allergic history, insomnia and pre-pregnancy BMI. Model 3 was additionally adjusted for season of delivery. Bold values denote statistical significance at the $p < 0.05$ level.

Abbreviations: BMI, body mass index; GWG, gestational weight gain; Q, quartile.

trimester than their peers. As there is a direct relationship between fetal growth and maternal GWG,[28,29] the finding of the current study was supported by other studies on fetal growth,[30,31] which indicate that fetuses with persistently low growth in the first two trimesters had a higher risk of developing asthma, obstructed lung function and requiring asthma medications than those with persistently high growth during the period. These suggest that early pregnancy may be a critical time window for the prevention of atopic allergy. Moreover, the association of GWG pattern characterised by rapid GWG earlier in pregnancy with a lower risk of offspring atopic allergy was more pronounced in mothers with low pre-pregnancy BMI. It is possible that underweight women were more likely to suffer from malnutrition, hence rapid GWG associated with sufficient nutrition supply and store early in pregnancy may benefit the development of the fetal immune system.[32] In this regard, underweight women should have relatively more GWG in their first two trimesters and lower GWG thereafter.

In the current study, no significant associations of GWG patterns with allergic contact dermatitis and food allergy in offspring were observed. To our knowledge, no prior study has evaluated these associations as we have here, although two studies have indicated that inadequate total GWG was associated with a lower risk of food allergy in children.[33,34] These findings may imply that the level of GWG, rather than the pattern of GWG, is an important factor for food allergy in offspring. The associations of maternal GWG with allergic contact dermatitis and food allergy in offspring require further investigation.

Although previous studies have suggested an association of extremely low or high GWG with the risk of allergic diseases,[9–12] the current study found that the main results were robust after excluding women with GWG of <5 kg or ≥20 kg, suggesting that the association of GWG patterns with offspring allergic diseases was not affected by extremely low or high total GWG. However, the association between the GWG pattern characterised by rapid GWG earlier in pregnancy and a lower risk of atopic allergy in offspring was significantly attenuated after adjustment for season of delivery, although the association remained statistically significant. These indicate that season of delivery, reflecting the seasons spanned by pregnancy, is an important confounding factor when evaluating the association of GWG patterns with allergic diseases in the offspring. Also, the association of GWG pattern characterised by rapid GWG earlier in pregnancy with a lower risk of atopic allergy was more pronounced in offspring born in winter or spring, which may be related to seasonal variation of vitamin D synthesis, nutrient intake, sleep patterns, etc.,[35–37] and more research is needed to explore the association.

The mechanism under the association of maternal GWG patterns with atopic allergy in offspring remains unclear, but the thymus may be involved. Atopic allergy reflects a persistent immunoglobulin E (IgE) response to common antigens and is linked to an imbalance of thymus-derived lymphocytes.[38] As a key organ of the human immune system, the thymus is known to be affected by malnutrition.[32] Previous studies have indicated an association between restricted fetal growth, as a measure of malnutrition in utero, and mismatched development of the thymus.[39,40] Moreover, early pregnancy is a critical window for the development of the thymus, the organogenesis of which is complete by 20 weeks of gestation.[41,42] The maternal GWG pattern characterised by rapid GWG earlier in pregnancy may be an indicator of sufficient maternal nutrition in the critical time window, which may benefit the normal development of fetal thymus and lower the risk of atopic allergy during infancy.

## 5 | CONCLUSION

In conclusion, the current study first evaluated the association of maternal GWG patterns with allergic diseases in offspring. Maternal GWG pattern characterised by rapid GWG earlier in pregnancy was found to be associated with a lower risk of atopic allergy but not of allergic contact dermatitis and food allergy in offspring.

### AUTHOR CONTRIBUTIONS

NY contributed to the conception and design of the research. GX, XY, LH, GS, and NY supervised the study conduct. XC, LH, CZ, MW, WW, HW, SY, XC and LL conducted the research. LL and LH analysed the data. LL and XC drafted the article. All authors provided intellectual input and contributed and approved the final version of the article for publication.

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### CONFLICT OF INTERESTS

None declared. Completed disclosure of interests form available to view online as supporting information.

### DATA AVAILABILITY STATEMENT

Data available on request from the authors.

### ETHICS APPROVAL

This study was performed in accordance with the Helsinki declaration. The study was approved by the ethics review committee of Tongji Medical College of Huazhong University of Science and Technology on 16 April 2013 (no. 201302), and all participants provided written informed consent at enrolment.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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