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Title page

Title

Prepregnancy BMI, Gestational Weight Gain and Risk of Childhood Atopic Dermatitis: A Systematic Review and Meta-Analysis.

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Running title

Maternal weight and childhood atopic dermatitis

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Abstract

Background: Maternal weight before and during pregnancy influences the health of offspring. Several observational studies have investigated a link between the risk of childhood atopic dermatitis (AD) and prepregnancy maternal body mass index (BMI) and gestational weight gain (GWG), but the conclusions of these studies were inconsistent. The aim of this review was to evaluate the association between the risk of childhood AD and prepregnancy maternal BMI and GWG.

Methods: The PubMed, Embase, Cochrane, Web of Science, and Scopus databases were searched from inception to February 2, 2021. Observational studies investigating the association between the risk of childhood AD and prepregnancy maternal BMI, GWG were included. Fixed- or random- effects models with inverse variance weights were used to calculate pooled risk estimates. Subgroup analysis and sensitivity analysis were used to explore the sources of heterogeneity.

Results: Thirteen studies with a total of 114,485 participants were included. Ten studies reported prepregnancy maternal BMI and five reported GWG. Maternal underweight was associated with a higher risk of childhood AD (odds ratio [OR]=1.06; 95% confidence interval [CI], 1.02-1.10). Continuous BMI was not related to childhood AD (OR = 1.00; 95% CI, 0.98-1.02). In comparison with normal GWG, moderate/very high GWG increased the risk of childhood AD (OR = 1.05; 95% CI, 1.02-1.08; OR = 1.13; 95% CI, 1.07-1.19, respectively) while low GWG decreased the

risk (OR = 0.92; 95% CI, 0.89-0.96). Excessive GWG relative to recommendations was associated with a higher risk of childhood AD (OR = 1.05; 95% CI, 1.01-1.10), while a lower risk of childhood AD was associated with inadequate GWG relative to recommendations (OR = 0.87, 95% CI: 0.83-0.91).

Conclusions: Maternal underweight, high GWG, and excessive GWG relative to recommendations are associated with an elevated risk of childhood AD, while low GWG and inadequate GWG relative to recommendations decreased the risk. Weight management before and during pregnancy is encouraged for primary prevention of childhood AD.

Key Messages

Several observational studies have investigated a link between the risk of childhood atopic dermatitis and prepregnancy maternal body mass index and gestational weight gain, but the conclusions of these studies were inconsistent. This systematic review and meta-analysis evaluates the association between the risk of childhood atopic dermatitis and prepregnancy maternal body mass index and gestational weight gain for the first time. Our results showed that maternal underweight, high gestational weight gain, and excessive gestational weight gain relative to recommendations are associated with an elevated risk of childhood atopic dermatitis, while low gestational weight gain and inadequate gestational weight gain relative to recommendations decreased the risk. Weight management before and during pregnancy is encouraged for primary prevention of childhood atopic dermatitis.

Keywords

Pregnancy; body mass index; gestational weight gain; childhood; atopic dermatitis; meta-analysis

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by pruritic, erythematous, and scaling lesions that affects up to 20% of children worldwide.¹ Fifty percent of AD cases are diagnosed in the first year of life, and 85% are diagnosed by 5 years of age.² The burden of symptoms influences the quality of life of children with AD and their families.^{3,4} Hereditary and environmental factors are presumed to cause AD. The risk factors for the development of AD in childhood include a family history of allergic diseases, living in an urban area, exposure to antibiotics, and a high-sugar diet.⁵ However, maternal factors (e.g. smoking exposure, breastfeeding, and maternal antibiotic consumption⁶) that affect the risk of AD in children have received increasing attention.^{7,8}

Maternal prepregnancy body mass index (BMI) and gestational weight gain (GWG) have various short- and long-term effects on the offspring. Increased maternal BMI is associated with an increased risk of infant death, and excessive and inadequate GWG are associated with a higher risk of adverse infant outcomes.^{9,10} Maternal overweight and underweight are related to metabolic disorders (e.g. obesity and diabetes), neurologic disorders (e.g. cognitive deficits and autism), and osteoporosis in offspring.¹¹ For allergic diseases, Liu et al.¹² performed a meta-analysis of 22 studies, and their results suggested that maternal obesity or overweight and high or low GWG increased the risk of asthma and wheeze in children. Gaillard et al.¹³ summarized previous studies and found that maternal obesity was not associated with other atopic diseases, including food allergies, AD, allergic rhinitis, and hay fever.

Several observational studies have investigated the link between the risk of childhood AD and prepregnancy maternal BMI and GWG, but their conclusions were inconsistent. Some studies reported that maternal BMI and GWG were not related to the risk of AD in children,^{14,15} while other studies showed a negative or positive association.¹⁶⁻¹⁸ Thus, the aim of this meta-analysis was to evaluate the association between the risk of childhood AD and prepregnancy maternal BMI and GWG. To examine this association, we reviewed the observational studies that assessed the risk of AD in children whose mothers had prepregnancy BMI and GWG that was either too high or too low in comparison with normal mothers.

Methods

In this meta-analysis, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement to complete the report (supplementary PRISMA checklist).¹⁹

We prospectively registered the protocol for this review in PROSPERO (CRD 42020218560).

Literature search and selection

We searched the PubMed, Embase, Cochrane, Web of Science, and Scopus databases from inception to February 2, 2021, with the following search query: (maternal OR mother OR prepregnancy OR pregnancy OR gestational) AND (obesity OR obese OR overweight OR body mass index OR BMI OR body weight OR weight gain) AND (child OR children OR childhood OR infant OR offspring) AND (Eczema OR atopic Dermatitis OR atopic disease OR atopy) using Medical Subject Heading terms and free text terms. After duplicates were removed, three authors (WSC, LW, and HY) selected the eligible studies independently by screening titles and abstracts and then read the full texts.

Inclusion and exclusion criteria

Studies were included if they reported the following contents: 1) Study participants: Children between birth and ≤ 18 years of age whose mothers' prepregnancy BMI and GWG data were available. 2) Study outcomes: AD during childhood, 3) Study design: Observational studies. 4) Studies written in English. We excluded: 1) duplicate reports, 2) conference abstracts, reviews, or editorials, 3) studies not published in English, 4) studies that did not differentiate between AD and other skin disorders, 5) studies that did not explore the association between the risk of childhood AD and prepregnancy maternal BMI and GWG, 6) non-observational studies, and 7) animal studies.

Data extraction

We extracted the following data: first author, year of publication, study design, study location,

sample size, age at outcome, BMI category, diagnostic criteria for AD, number of participants with and without AD, risk estimates, main conclusions, and adjusted covariates. Disagreements between three authors (WSC, LW and HY) on the literature selection and data extraction were resolved by mutual discussions and consultation with a fourth author (WXZ).

Quality evaluation

The quality of the included studies was assessed by using the Newcastle-Ottawa Scale (NOS) for cohort studies.²⁰ Studies with ≥ 7 stars on the NOS were considered to be of high quality. The Agency for Health Care Research and Quality (AHRQ) tool was applied to evaluate cross-sectional studies. Studies with ≥ 8 points on the AHRQ tool were considered to be of high quality.

Statistical analysis

In this meta-analysis, we divided BMI categories into four groups as follows: underweight, normal, overweight, and obese. Fixed- or random- effects models with inverse variance weights were used to calculate pooled risk estimates. GWG categories included low GWG (<10 kg), normal GWG (10-15 kg), moderate-high GWG (15-20 kg), and very-high GWG (>25 kg). Heterogeneity of the data was assessed by the I^2 measure of inconsistency (less than 25%: no heterogeneity; 25%-49%: low heterogeneity; 50%-75%: moderate heterogeneity; more than 75%: high heterogeneity). If there was significant heterogeneity, we used random-effects models for the meta-analysis and performed subgroup and sensitivity analyses to explore the source of heterogeneity. Publication bias was evaluated by using Egger's test. $P < 0.05$ was considered significant. All statistical analyses were performed in Stata version 14 (Stata Corp, College Station, TX).

Results

Search results

As shown in **Figure 1**, a total of 1,597 records were identified: 263 from PubMed, 568 from

Embase, 95 from Cochrane, 296 from Web of Science, and 375 from Scopus. According to the inclusion and exclusion criteria, 13 studies^{14-18,21-28} were included in the research and 12 studies^{15-18,21-28} were included in the meta-analysis.

Study characteristics and quality assessment

The main characteristics of the included studies are shown in **Table 1** (the specific data are provided in the supporting information: supplementary specific study characteristics). A total of 13 studies^{14-18,21-28} with a total of 114,485 participants were included in this systematic review and meta-analysis. Sample sizes ranged from 339 to 38,874 participants, and age at outcome ranged from 6 months to 17 years old. Among the included studies, 11 were cohort studies^{14-16,18,21-28} and 2 were cross-sectional studies.^{17,21} The studies were performed in Chile (1 study²⁷), China (1 study¹⁷), Denmark (1 study¹⁵), Finland (1 study¹⁴), Japan (2 studies^{16,21}), Sweden (2 studies^{24,25}), the UK (1 study²⁶) and the USA (4 studies^{18,22,23,28}). For maternal BMI and GWG, 5 studies^{17,24-28} used medical records, and 8 studies^{14-18,21-23} used self-reports, questionnaires or questions. A total of 7 studies^{15,17,18,23,24,27,28} reported prepregnancy BMI, 4 studies^{16,21,22,25,26} reported continuous BMI, 3 studies^{15,17,18} reported GWG, 2 studies^{17,18} reported GWG relative to recommendations and 1 study¹⁴ reported maternal weight gain in quartiles (not included in the meta-analysis). For the diagnostic criteria of AD, 2 studies^{23,28} used medical records, and 10 studies^{14-18,21,22,24-27} used questionnaires or questions. Quality assessment results are reported in Table 1. For cohort studies, 5 studies^{15,16,18,23,25,26} received 7 stars, 4 studies^{14,22,27,28} received 6 stars, and 1 study²⁴ received 5 stars. For cross-sectional studies, 2 studies^{17,21} received a score of 6.

Prepregnancy maternal BMI categories and the risk of childhood AD

A total of 7 of the 11 studies^{15,17,18,23,24,27,28} were included in this meta-analysis (4 studies provided risk estimates and 3 provided the number of cases; the studies included in the meta-analysis are classified in the supporting information: supplementary study classification). **Figure 2** shows the pooled OR for AD in offspring classified by BMI category. In comparison with children whose mothers were of normal weight, those whose mothers were underweight had a higher risk of AD (OR = 1.06; 95% CI, 1.02-1.10) with low heterogeneity ($I^2 = 38.2\%$). For maternal overweight,

those whose mothers were overweight had a lower risk of AD (OR = 0.91; 95% CI, 0.88-0.94) with low heterogeneity ($I^2 = 45.6\%$), and maternal obesity showed the same trends (OR = 0.87; 95% CI, 0.85-0.90) with high heterogeneity ($I^2 = 86.7\%$).

Exploration of heterogeneity: The results of subgroup analyses (based on study design, geographic locations, age, case number, ascertainment of maternal weight, ascertainment of AD, study quality, and risk estimate source for categorical BMI) are shown in **Table 2**. Figure S1 shows the results of the sensitivity analysis based on maternal BMI categories.

For maternal obesity, the tests for subgroup differences were significant in all subgroups. The results of the study subsets (cross-sectional study subsets; non-US studies; age, 0-2 yr and 12-18 yr; case number <10,000; ascertainment of maternal weight using non-medical records; ascertainment of AD using non-medical records; high-quality studies; and risk-estimate source provided in the included studies) showed that maternal obesity was not associated with the risk of childhood AD. Sensitivity analysis did not determine the source of heterogeneity as shown in **Figure S1**.

For maternal overweight, the results of the study subsets (age: 0-2 yr, 6-12 yr, 12-18 yr; ascertainment of maternal weight using non-medical records; ascertainment of AD using non-medical records; high-quality studies; and risk-estimate source provided in included studies) suggested that maternal overweight was not related to the risk of childhood AD. The sensitivity analysis indicated that the study by Castro-Rodriguez et al.²⁷ might be a source of heterogeneity as shown in **Figure S1**.

For maternal underweight, the results of the cross-sectional study subsets (one study) indicated that maternal underweight was not associated with the risk of childhood AD. Sensitivity analysis did not determine the source of heterogeneity as shown in **Figure S1**.

Publication bias analysis was not evaluated because of the small number of studies ($n = 7$, less than 10)

Continuous BMI and the risk of childhood AD

A total of 5 studies^{16,21,22,25,26} were included in this meta-analysis (the studies included in the meta-

analysis are classified in the supporting information: supplementary-study classification). As shown in **Figure S2**, continuous BMI was not associated with AD (OR = 1.00; 95% CI, 0.98-1.02) with high heterogeneity ($I^2 = 75.5\%$).

Exploration of heterogeneity: The results of subgroup analyses (based on study design, geographic locations, age, case number, ascertainment of maternal weight, ascertainment of AD, continuous BMI category, and study quality for continuous BMI) are shown in **Table S1**. Significant subgroup differences in the subgroup analyses were found for geographic locations, age, case number and ascertainment of maternal weight. For the subgroup analysis, the results of the study subsets (geographic locations: Japan; age: 0-2 yr; case number: > 3000; ascertainment of maternal weight: Non-medical records) were consistent with the overall results. Sensitivity analysis did not determine the source of heterogeneity as shown in **Figure S3**.

Publication bias analysis was not evaluated because of the small number of studies (n=5).

GWG categories and the risk of childhood AD

A total of 3 studies^{15,17,18} were included in this meta-analysis (GWG converted to kilograms; the studies included in the meta-analysis are classified in the supporting information: supplementary study classification). **Figure 3** shows that moderate-high GWG (15-25 kg) increased the risk of childhood AD (OR = 1.05; 95% CI, 1.02-1.08) with moderate heterogeneity ($I^2 = 63.8\%$), and very-high GWG (> 25 kg) showed the same trends (OR = 1.13; 95% CI, 1.07-1.19) with low heterogeneity ($I^2 = 36.7\%$) while low GWG (< 10 kg) decreased the risk (OR = 0.92; 95% CI, 0.89-0.96) with no heterogeneity ($I^2 = 10.4\%$).

Subgroup analysis, sensitivity analysis, and publication bias analysis were not conducted because of the small number of studies (n = 3).

GWG relative to recommendations and the risk of childhood AD

As shown in **Figure 4**, 2 studies^{17,18} were included in this meta-analysis (the studies included in the meta-analysis are classified in the supporting information: supplementary study classification).

In comparison with adequate GWG, excessive GWG was associated with a higher risk of childhood AD (OR = 1.05; 95% CI, 1.01-1.10) with no heterogeneity ($I^2 = 0.00\%$) while a lower risk of childhood AD was associated with inadequate GWG (OR = 0.87, 95% CI: 0.83-0.91) with low heterogeneity ($I^2 = 32.8\%$).

Subgroup analysis, sensitivity analysis, and publication bias analysis were not conducted because of the small number of studies ($n = 2$).

Discussion

Summary of the main results

Our meta-analysis found that maternal underweight, high GWG, and excessive GWG relative to recommendations are associated with an elevated risk of childhood AD, while low GWG and inadequate GWG relative to recommendations decreased the risk. Although maternal overweight was associated with a lower risk of AD, and maternal obesity showed the same trends, subgroup analysis indicated that the overall results were unreliable.

Comparison with the previous literature

To our knowledge, this meta-analysis is the first to evaluate the association between the risk of childhood AD and prepregnancy maternal BMI and GWG. We found that maternal underweight was associated with a higher risk of AD in offspring and that maternal obesity might not be related to the risk. Gaillard et al.¹³ summarized relevant studies before 2016 and found that maternal obesity was not associated with AD. We comprehensively searched the relevant studies in five databases, including studies published in 1935-2021, and pooled risk estimates. In comparisons for asthma/wheezing,¹² high GWG was shown to increase the risk of asthma/wheezing and AD in children. Low GWG decreased the risk of AD but increased the risk of asthma/wheezing, which indicated that abnormal GWG had different roles in the pathogenesis of asthma/wheezing and AD. On the basis of these results, we speculated that a high proportion of weight gain during pregnancy increased the risk of AD in children, especially in mothers who were underweight.

Exploration of heterogeneity

Significant heterogeneity was detected in one subgroup of maternal BMI categories (maternal

obesity: $I^2 = 86.7\%$) and continuous BMI ($I^2 = 59.4\%$). This heterogeneity may have been derived from confounding factors, such as study design, study location, sample size, age, case number, ascertainment of maternal weight, ascertainment of AD, study quality, risk estimate source, and continuous BMI categories. For maternal obesity, we found that study design, study location, age, case number, ascertainment of maternal weight, ascertainment of AD, study quality, and risk-estimate source might have caused inconsistencies in studies after subgroup analysis. We also conducted subgroup analyses for maternal overweight and underweight, which indicated that ascertainment of maternal weight, ascertainment of AD, study quality, and risk-estimate source might be the causes of heterogeneity. Most notably, different risk-estimate sources led to different results. For maternal overweight and obesity, the results of the study subsets of risk-estimate sources provided in the included studies were inconsistent with the overall results. The risk estimates calculated by case number lacked consideration for confounding factors, which indicated that the overall results showing that maternal overweight and obesity were associated with a lower risk of childhood AD were unreliable. For continuous BMI, geographic locations, age, case number and ascertainment of maternal weight also caused heterogeneity. Sensitivity analysis did not determine the source of heterogeneity in maternal categorical BMI groups or continuous BMI. This exploration of heterogeneity provided a topic of research for later studies.

Implications for research

The present findings suggest several directions for future research. High-quality prospective cohort studies with large sample sizes that are performed in different countries will improve the robustness of the available evidence. For ascertainment of maternal weight and AD, medical records or other reliable methods are recommended in comparison studies based on self-reports, questionnaires, and questions, which may be affected by causing recall bias. Considering the different clinical manifestations, the prevalence of AD in different age groups (0-2 yr, 2-6 yr, 6-12 yr, 12-18 yr) deserves attention. In all studies included, the severity of AD was not classified, and evaluation of the clinical score and quality of life in children with AD should be under consideration. For the assessment of maternal weight, GWG and GWG relative to recommendations might not be comprehensive enough, and we suggest that the proportion of weight gain in comparison with prepregnancy weight could be used to evaluate the weight gain rate during pregnancy. In addition, we suggest combining maternal BMI and GWG to investigate the relationship (e.g. underweight with adequate/inadequate/excessive GWG). The

effects of GWG in different trimesters of pregnancy are also worth exploring. The assessment of maternal weight status before delivery requires an appropriate evaluation method.

Implications for prepregnancy and pregnancy management

Our meta-analysis investigated the relationship between the risk of childhood AD and prepregnancy maternal BMI, and GWG. The results indicate that weight management before and during pregnancy should not be ignored, including weight management of mothers who are underweight. The American College of Obstetricians and Gynecologists recommends a total weight gain of 28-40 lb (12.7-18.1 kg) for underweight women, 25-34 lb (11.3-15.4 kg) for normal-weight women, 15-25 lb (6.8-11.3 kg) for overweight women, and 11-20 lb (5.0-9.1 kg) for obese women.²⁹ Our results suggested that for underweight women, a total weight gain under 15 kg but in the recommended range might prevent AD in children. During pregnancy preparation, weight gain to meet the normal BMI in underweight women for the prevention of AD in children needs to be tested. Evaluation of nutrient status alongside weight management deserves some attention for better understanding of the influence of maternal weight. In addition, weight management in women with obesity or overweight is strongly recommended to reduce the risk of adverse maternal and infant outcomes.

Strengths and limitations

Our meta-analysis had the following advantages. 1) This systematic review and meta-analysis evaluates the association between the risk of childhood AD and prepregnancy maternal BMI, GWG for the first time. 2) Our meta-analysis was mostly based on prospective birth cohort studies, and recall bias and selection bias minimally affected the results. 3) Subgroup analyses indicates that several potential factors interfered with the results and provides suggestions for future research. 4) Obesity and maternal obesity have received much attention, and maternal underweight is less common in developed societies. It is important not to forget the effect of maternal underweight on children's health. Mothers who are underweight need to avoid excessive weight gain during pregnancy.

Nevertheless, several limitations of this meta-analysis should be acknowledged. 1) In our meta-analysis, we excluded conference abstracts and non-English language papers, which might introduce publication bias. 2) Several risk estimates were calculated by the case number lacking consideration for confounding factors, which led to unreliable overall results. 3) For continuous

BMI, GWG, and GWG relative to recommendations, fewer than 5 studies were included, and the overall result might be affected by individual studies. More studies are needed. 4) Because of limited information on race/ethnicity in the included studies, we could not extract this information.

Conclusions

The results of this meta-analysis indicated that maternal underweight, high GWG, and excessive GWG relative to recommendations are associated with an elevated risk of childhood AD, while low GWG and inadequate GWG relative to recommendations decreased the risk. Weight management before and during pregnancy is encouraged for primary prevention of childhood AD. Clinical trials of maternal weight management and more high-quality prospective cohort studies are needed.

Acknowledgments

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Impact statement

We conducted this meta-analysis to evaluate the association between the risk of childhood atopic dermatitis and prepregnancy maternal body mass index and gestational weight gain. There are several strengths in our study. First, this systematic review and meta-analysis evaluated the association between the risk of childhood atopic dermatitis and prepregnancy maternal body mass index and gestational weight gain for the first time. Second, subgroup analysis indicated several potential factors interfering with the results. Third, our results showed that maternal underweight, high gestational weight gain and excessive gestational weight gain relative to recommendations are associated with an elevated risk of childhood atopic dermatitis, while low gestational weight gain and inadequate gestational weight gain relative to recommendations decreased the risk. Fourth, our work indicates that weight management before and during pregnancy is encouraged for the primary prevention of childhood atopic dermatitis.

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Figure legends

Figure 1. PRISMA flow chart of the included studies for the meta-analysis. A total of 1,597 articles were identified: 263 from PubMed, 568 from Embase, 95 from Cochrane, 296 from Web of Science, and 375 from Scopus. A total of 575 reviews/conference abstracts/editorials/case reports, 44 non-English studies, 10 animal studies, 109 non-observational studies and 456 on irrelevant topics were excluded. Then, 156 studies were removed after reading the full texts. Finally, 13 studies were included in the study, and 12 studies were included in the meta-analysis.

Figure 2. The pooled risk estimates by maternal BMI category. In comparison with normal maternal weight, maternal underweight was associated with a higher risk of AD while maternal overweight was associated with a lower risk of AD, with maternal obesity showing the same trends. The category of maternal obesity showed high heterogeneity.

Figure 3. The pooled risk estimates by GWG category. In comparison with children whose mothers were of normal GWG, moderate-high GWG (15-25 kg) increased the risk of childhood AD and very-high GWG (>25 kg) showed the same trends, while low GWG (<10 kg) decreased the risk of childhood AD. The category of moderate-high GWG showed moderate heterogeneity.

Figure 4. The pooled risk estimates by GWG relative to recommendation category. In comparison with children whose mothers had adequate GWG, excessive GWG was associated with a higher risk of childhood AD while inadequate GWG was associated with a lower risk of childhood AD.

Supporting information

Supplementary **Figure S1.** The results of sensitivity analysis based on maternal BMI category (A: maternal obesity, B: maternal overweight, C: maternal underweight).

Supplementary **Figure S2.** The pooled risk estimates by continuous BMI. Continuous BMI was not associated with the risk of childhood AD.

Supplementary **Figure S3.** The results of sensitivity analysis based on continuous BMI.

Supplementary **Table S1.** Summary of subgroup analysis results for continuous BMI

Supplementary PRISMA checklist

Supplementary specific study characteristics

Supplementary study classification

Table 1 Characteristics and quality assessment of studies on the association between prepregnancy BMI, GWG and childhood AD.

First author, year	Study design	Study location	Sample size	Age	Ascertainment of maternal weight	Maternal weight categories	Ascertainment of AD	Main conclusions	Quality assessment
Xu, 1999 ¹⁴	cohort study	Finland	8088	7 yr	questionnaire	GWG	questionnaire	Maternal weight gain was not associated with AD in offspring ($P=0.410$).	6 stars
Ushiyama, 2002 ²¹	cross-sectional study	Japan	2070	7.6±2.8 yr	questionnaire	continuous BMI	questionnaire	Maternal continuous BMI (1kg/m ² increase) was not associated with AD in offspring (OR=1.06, 95% CI, 0.98-1.14).	6 scores
Moore, 2004 ²²	cohort study	USA	1005	6 mo	question	continuous BMI	question	Maternal continuous BMI (1kg/m ² increase) was not associated with AD in	6 stars

								offspring (OR=1.01,95% CI, 0.98-1.05).	
Kumar, 2010 ²³	cohort study	USA	1191	6 yr	questionnaire	prepregnancy BMI	medical record	Maternal overweight and obesity were not associated with AD in offspring (OR=0.91,95% CI, 0.67-1.23, OR=0.98,95% CI, 0.69-1.39, respectively).	7 stars
Lundholm, 2010 ²⁴	cohort study	Sweden	10132	9 yr/12 yr	medical record	prepregnancy BMI	question	There was no clear relationship between the rate of atopic eczema and the mother's BMI at the beginning of the pregnancy.	5 stars

Harpsøe, 2013 ¹⁵	cohort study	Denmark	38874	7 yr	self-reported and question	prepregnancy BMI GWG	questionnaires	BMI and GWG were not significantly associated with AD.	7 stars
Ekström, 2015 ²⁵	cohort study	Sweden	3294	16 yr	medical record	continuous BMI	questionnaires	No statistically significant associations were found for the association between maternal continuous BMI (5kg/m ² increase) and eczema (OR=1.03, 95% CI, 0.93–1.14).	7 stars
El-Heis, 2016 ²⁶	cohort study	UK	467	12 mo	medical record	continuous BMI	questionnaires	Maternal continuous BMI (1kg/m ² increase) was associated with increased risk of AD (OR=1.07, 95% CI, 1.03-1.13)	7 stars
Goudarzi, 2018 ¹⁶	cohort study	Japan	3296	1 yr, 2 yr, 4 yr, 7 yr	questionnaire	continuous BMI	questionnaires	Maternal continuous BMI (1kg/m ² increase)	7 stars

				yr					was associated with decreased risk of AD at age 7(OR=0.97, 95% CI, 0.94-0.99)	
Drucker, 2019 ¹⁸	cohort study	USA	13269	17 yr	questionnaires	prepregnancy BMI GWG relative to recommendations	question	Maternal prepregnancy BMI was not associated with AD (P= 0.48). Compared to children of mothers who gained 25–34 lb, children of mothers who gained more than 45 lbs (OR=1.23, 95% CI, 1.05–1.43) had an increased risk of AD. GWG relative to recommendations was not associated with AD (under	7 stars	

									recommendations: OR=0.94, 95% CI, 0.82–1.07; over recommendations: Over recommendations: OR=1.08, 95% CI, 0.96–1.20)	
Castro-Rodriguez, 2020 ²⁷	cohort study	Chile	339	30 mo	medical record	prepregnancy BMI	question		Maternal obesity was associated with increased risk of AD at age 24mo ($P=0.025$)	6 stars
Chen, 2020 ¹⁷	cross-sectional study	China	15145	3-14 yr	questionnaire(prepregnancy BMI) questionnaire and medical record(GWG)	prepregnancy BMI GWG GWG relative to recommendations	questionnaire		Maternal prepregnancy BMI was not associated with AD ($P= 0.35$). Compared to children of mothers who gained 10-15 kg, children of mothers who gained less than 10 kg had an	6 scores

decreased risk of AD (OR=0.89, 95% CI, 0.84-0.94) and children of mothers who gained more than 15 kg had an increased risk of AD (OR=1.09, 95% CI, 1.04-1.13; OR=1.15, 95% CI, 1.07-1.24). GWG under recommendations was associated with lower risk of AD (OR=0.86 , 95% CI, 0.82-0.91) and GWG over recommendations was associated with higher risk of AD (OR=1.05 ,

95% CI, 1.01-1.10)									
Richards, 2020 ²⁸	cohort study	USA	17315	4 yr	medical record	prepregnancy BMI	medical record	Available data but no relevant conclusions.	6 stars

BMI: maternal body mass index; GWG: gestational weight gain; AD: atopic dermatitis.

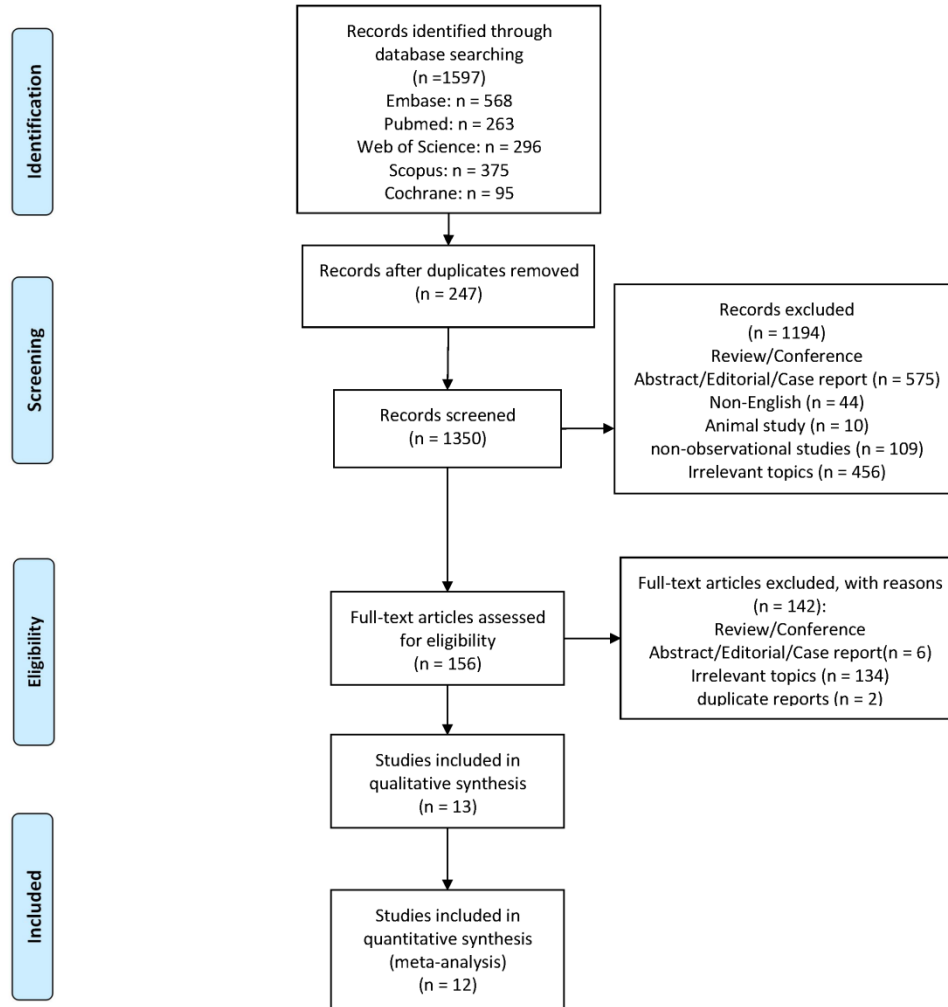
Table 2. Summary of subgroup analysis results for categorical BMI

Categorical BMI	Subgroup	Number of studies	OR (95% CI)	I^2 (P value)	$P_{\text{heterogeneity between groups}}$
Maternal obesity	Study design	7	0.87(0.85-0.90)	86.7%(0.000)	-
	Cross-sectional study	1	0.98(0.92-1.04)	-	0.000
	Cohort study	6	0.84(0.81-0.87)	82.4%(0.000)	
	Geographic locations				
	USA	3	0.81(0.79-0.84)	35.3%(0.213)	0.000
	Non-USA	4	0.99(0.94-1.04)	69.3%(0.011)	
	Age				
	0-2 yr	1	2.43(1.26-4.68)	-	0.000
	2-6 yr	2	0.81(0.78-0.84)	11.1%(0.289)	
	6-12yr	2	0.98(0.90-1.07)	65.2%(0.057)	
	12-18 yr	1	0.99(0.75-1.30)	-	
	3-14 yr	1	0.98(0.92-1.04)	-	
	Case number				
	> 10,000	5	0.87(0.84-0.89)	88.3%(0.000)	0.042
	≤10,000	2	1.20(0.88-1.63)	82.5%(0.000)	
	Ascertainment of maternal weight				
	Non-medical records	4	0.98(0.93-1.03)	16.0%(0.313)	0.000
	Medical records	3	0.82(0.79-0.85)	88.7%(0.000)	
	Ascertainment of AD				
	Non-medical records	5	0.99(0.94-1.04)	61.7%(0.023)	0.000
	Medical records	2	0.81(0.78-0.84)	11.1%(0.289)	
	Study quality				
	Low	3	0.86(0.83-0.89)	92.8%(0.000)	0.012

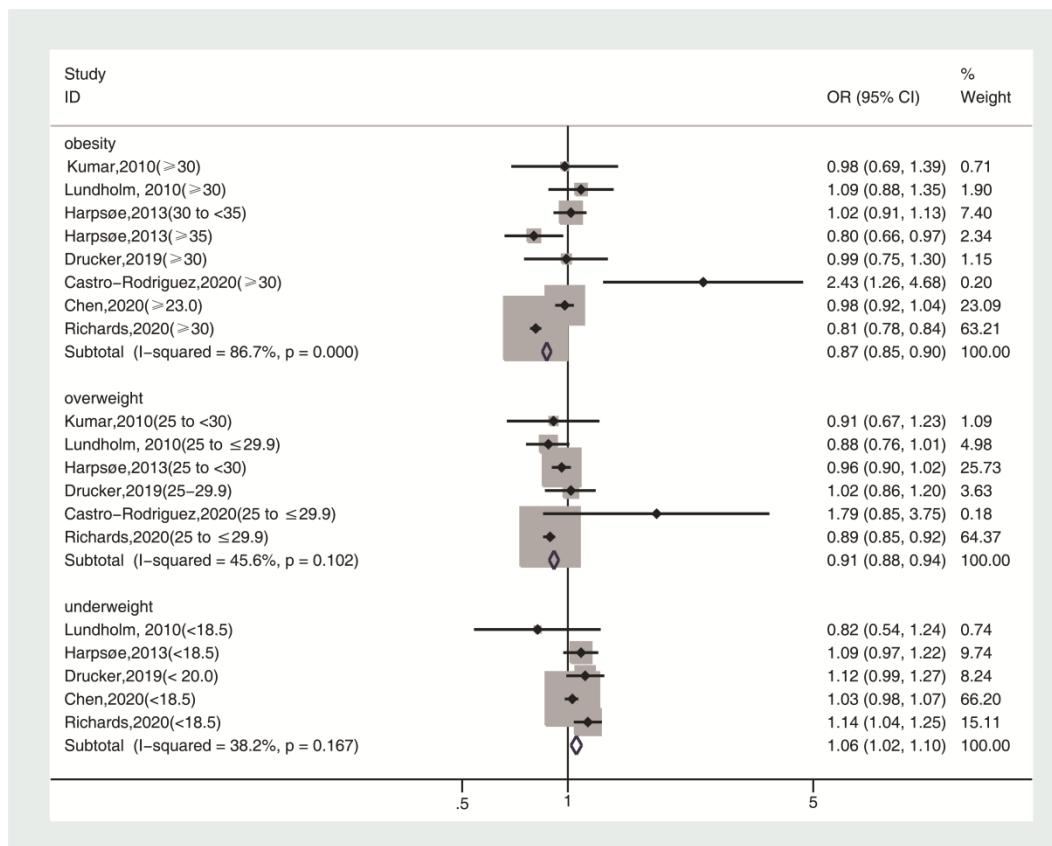
Maternal overweight	High	4	0.97(0.89-1.05)	36.1%(0.196)	
	Risk estimate source				
	Provided in the included studies	4	0.98(0.93-1.03)	16.0%(0.313)	0.000
	Not provided in the included studies	3	0.82(0.79-0.85)	88.7%(0.000)	
	Study design				
	Cross-sectional	0	-	-	-
	Cohort study	6	0.91(0.88-0.94)	45.6%(0.102)	
	Geographic locations				
	USA	3	0.90(0.86-0.93)	18.2%(0.294)	0.099
	Non-USA	3	0.99(0.94-1.04)	50.2%(0.135)	
	Age				
	0-2 yr	1	1.79(0.85-3.76)	-	0.047
	2-6 yr	2	0.89(0.86-0.93)	0.0%(0.887)	
	6-12 yr	2	0.095(0.89-1.00)	17.0%(0.272)	
	12-18 yr	1	1.02(0.86-1.20)	-	
	Case number				
	> 10,000	4	0.91(0.88-0.94)	50.2%(0.111)	0.510
	≤10,000	2	1.00(0.76-1.33)	63.5%(0.098)	
	Ascertainment of maternal weight				
	Non-medical records	3	0.97(0.91-1.02)	0.0%(0.743)	0.023
	Medical records	3	0.89(0.86-0.93)	41.6%(0.180)	
	Ascertainment of AD				
	Non-medical records	4	0.96(0.91-1.01)	35.4%(0.200)	0.033
	Medical records	2	0.89(0.86-0.93)	0.0%(0.887)	
	Study quality				

Maternal underweight	Low	3	0.89(0.88-0.93)	41.6%(0.180)	0.023
	High	3	0.97(0.91-1.02)	0.0%(0.743)	
	Risk estimate source				
	Provided in the included studies	3	0.97(0.91-1.02)	0.0%(0.743)	0.023
	Not provided in the included studies	3	0.89(0.86-0.93)	41.6%(0.180)	
	Study design				
	Cross-sectional	1	1.03(0.99-1.08)	-	0.046
	Cohort study	4	1.11(1.05-1.18)	0.0%(0.480)	
	Geographic locations				
	USA	3	1.12(1.04-1.21)	13.1%(0.316)	0.067
	Non-USA	2	1.04(1.00-1.08)	0.0%(0.366)	
	Age				
	2-6yr	1	1.14(1.04-1.25)	-	0.188
	6-12 yr	2	1.07(0.96-1.19)	40.3%(0.0196)	
	12-18 yr	1	1.12(0.99-1.27)	-	
	3-14 yr	1	1.03(0.99-1.08)	-	
	Case number				
	>10,000	5	1.06(1.02-1.10)	38.2%(0.167)	-
	≤10,000	0	-	-	
	Ascertainment of maternal weight				
	Non-medical records	3	1.05(1.01-1.09)	5.9%(0.743)	0.153
	Medical records	2	1.12(1.03-1.23)	56.5%(0.129)	
	Ascertainment of AD				
	Non-medical records	4	1.04(1.00-1.08)	12.4%(0.331)	0.081
	Medical records	1	0.89(0.86-0.93)	-	

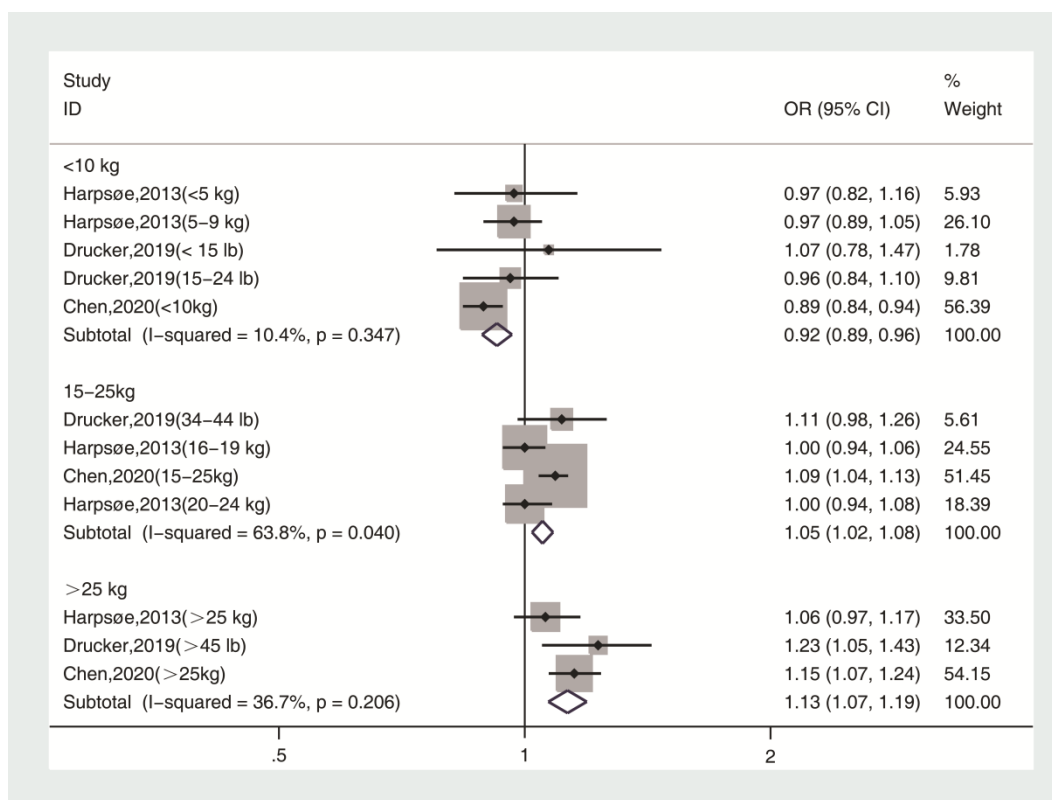
Study quality					
Low	3	1.05(1.01-1.09)	61.2%(0.076)	0.270	
High	2	1.10(1.01-1.20)	0.0%(0.753)		
Risk estimate source					
Provided in the included studies	2	1.04(1.00-1.08)	0.0%(0.366)	0.067	



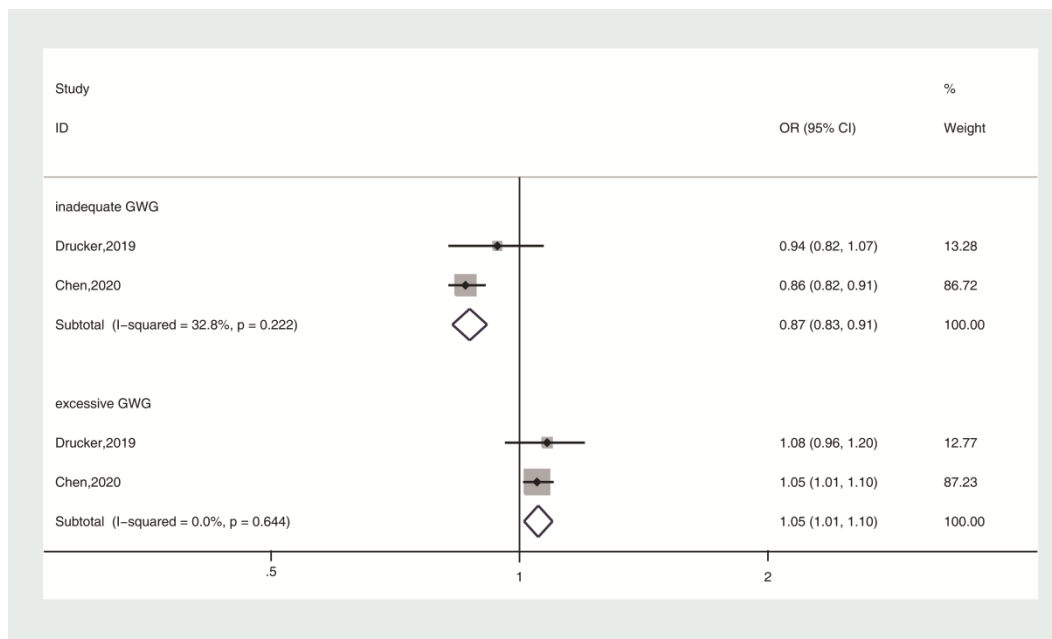
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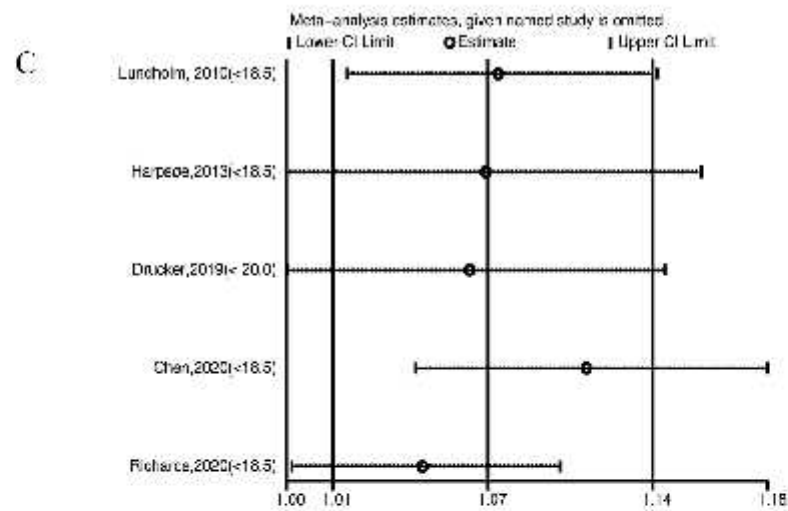
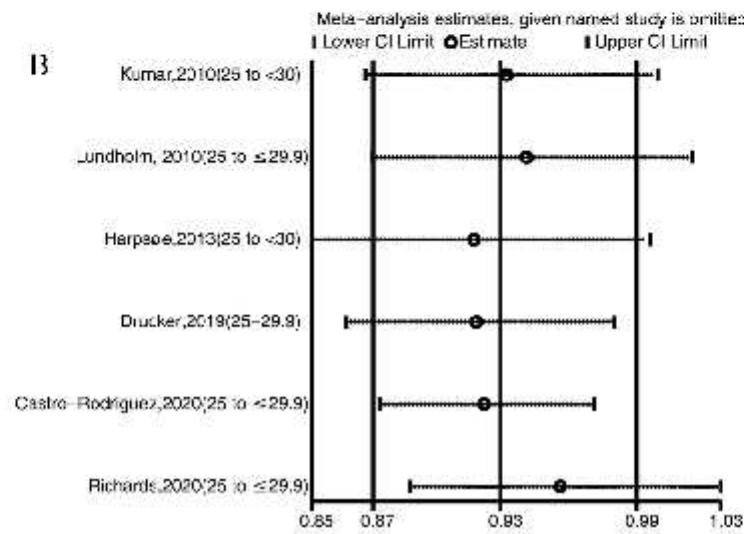
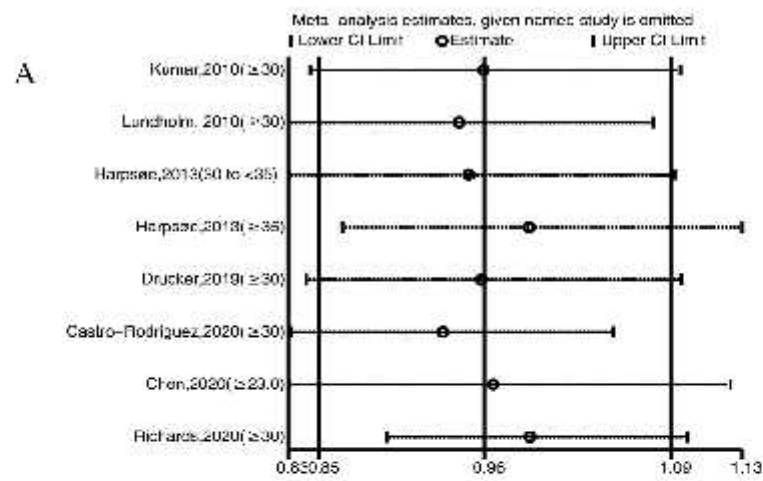
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pai_13488_f3.tif



pai_13488_f4.tif



Study				%
ID	OR (95% CI)			Weight

Ushiyama,2002		1.06 (0.98, 1.14)	5.70
Moore,2004		1.01 (0.98, 1.05)	27.40
El-Heis,2016		1.07 (1.03, 1.13)	15.19
Ekström,2015		1.03 (0.93, 1.14)	3.15
Goudarzi,2018		0.97 (0.94, 0.99)	48.56
Overall (I-squared = 75.5%, p = 0.003)		1.00 (0.98, 1.02)	100.00

.9

1

1.2

Meta-analysis estimates, given named study is omitted

■ Lower CI Limit

● Estimate

■ Upper CI Limit

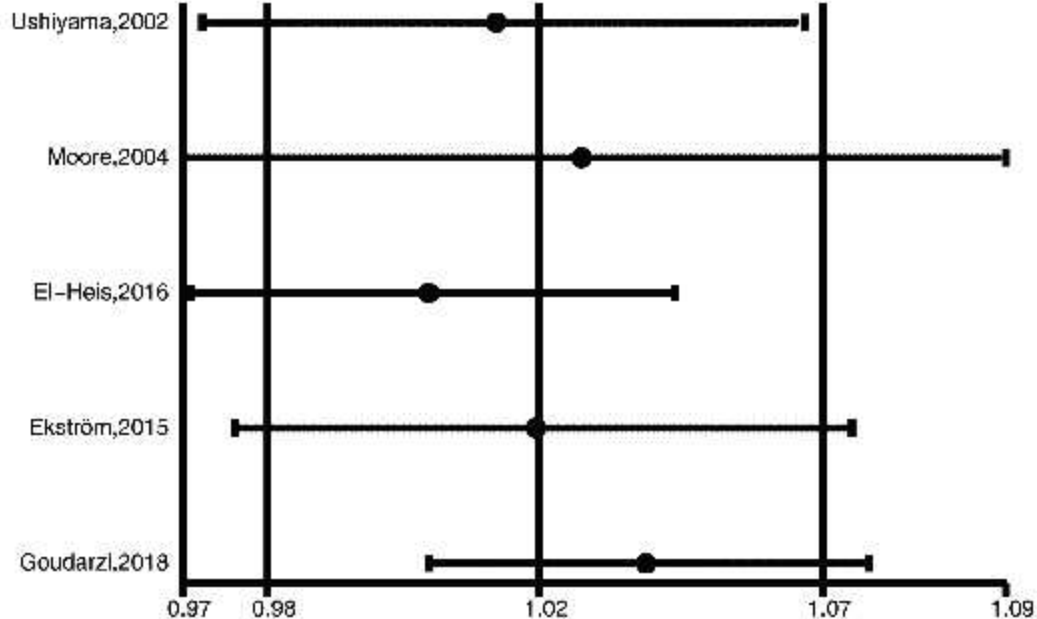


Table S1 Summary of subgroup analysis results for continuous BMI

Subgroup	Number of studies	OR(95%CI)	I^2 (P value)	$P_{\text{heterogeneity between groups}}$
Study design	5	1.00(0.98-1.02)	75.5%(0.003)	-
Cross-sectional study	1	1.06(0.98-1.14)	-	0.136
Cohort study	4	1.00(0.98-1.02)	78.8%(0.003)	
Geographic locations				
Japan	2	0.98(0.96-1.00)	78.9%(0.030)	0.005
Non-Japan	3	1.03(1.00-1.06)	47.8%(0.147)	
Age				
0-2 yr	2	1.03(1.00-1.06)	73.9%(0.050)	0.020
2-12yr	2	0.98(0.96-1.00)	78.9%(0.030)	
12-18 yr	1	1.03(0.93-1.14)	-	
Case number				
> 3000	2	0.97(0.95-1.00)	20.3%(0.263)	0.001
≤3000	3	1.03(1.01-1.06)	53.4%(0.117)	
Ascertainment of maternal weight				
Non-medical records	3	0.99(0.97-1.01)	70.6%(0.033)	0.003
Medical records	2	1.06(1.02-1.11)	0.0%(0.504)	
Ascertainment of AD				
Non-medical records	5	1.00(0.98-1.02)	75.5%(0.003)	-
Medical records	0	-	-	
Continuous BMI categories				
1kg/m ² increase in BMI	4	1.00(0.98-1.02)	81.3%(0.001)	0.598
5kg/m ² increase in BMI	1	1.03(0.93-1.14)	-	
Study quality				
Low	2	1.02(0.99-1.05)	23.0%(0.255)	0.227
High	3	0.99(0.97-1.02)	85.3%(0.001)	



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4,5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5,6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5,6



PRISMA 2009 Checklist

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5,6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	5,6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	7,8,9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Supplementary specific study characteristics
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7,8,9, Figure 2,3,4, Figure S2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	7,8,9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	7,8,9, Figure S1, S3, Table 2, Table S1
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	9
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11,12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10,11,12



PRISMA 2009 Checklist

FUNDING				
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.		1,12

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Table Specific characteristics and quality assessment of studies on the association between prepregnancy BMI, GWG and childhood AD.

First author, year	Study design	Study location	Sample size	Age	Ascertainment of maternal weight	Ascertainment of AD	Quality assessment	Maternal weight category	Comparison	O	R	ll	ul	Participants with AD in each group(n)	Participants without AD in each group(n)	Adjusted covariates
Xu,1999	cohort study	Finland	8088	7 yr	questionnaire	questionnaire	6 stars	maternal weight gain, in quartiles	First (lowest)	not included in the meta-analysis				118	1780	NA
Xu,1999	cohort study	Finland	8088	7 yr	questionnaire	questionnaire	6 stars	maternal weight gain, in quartiles	Second					117	1790	
Xu,1999	cohort study	Finland	8088	7 yr	questionnaire	questionnaire	6 stars	maternal weight gain, in quartiles	Third					133	1767	
Xu,1999	cohort study	Finland	8088	7 yr	questionnaire	questionnaire	6 stars	maternal weight gain, in quartiles	Fourth (highest)					138	1764	
Ushiyama,2002	cross-sectional	Japan	20708	7.6±2.0 yr	questionnaire	questionnaire	6 scores	continuous BMI	1kg/m2 increase in BMI	1.06	0.98	1.14		84	1824	Adjusted for family history,

	study														sex, order of birth and age of infants.
Moore,2004	cohort study	USA	1005	6 mo	question	question	6 stars	continuous BMI	1kg/m2 increase in BMI	1.01	0.98	1.05	172	833	Adjusted for gestational age at birth, birth weight for gestational age (z value), and infant gender; maternal age, race/ethnicity, education, and history of eczema; and home cockroach exposure.
Kumar,2010	cohort study	USA	1191	6 yr	questionnaire	medical record	7 stars	prepregnancy BMI	18.5 to <25(reference)				190	261	Adjusted for children's age, sex, maternal race (black/white/Hispanic/other), maternal education (<high school, high
Kumar,2010	cohort study	USA	1191	6 yr	questionnaire	medical record	7 stars	prepregnancy BMI	25 to <30	0.91	0.67	1.23	129	202	
Kumar,2010	cohort study	USA	1191	6 yr	questionnaire	medical record	7 stars	prepregnancy BMI	≥30	0.98	0.69	1.39	86	120	

															school, >high school), maternal history of atopic diseases (including food allergy, atopic dermatitis, asthma, and hay fever), parity (0, 1), premature delivery (<37 weeks), FGR, and LGA
Lundholm, 2010	cohort study	Sweden	10132	9 yr/12 yr	medical record	question	5 stars	prepregnancy BMI	<18.5	0.82	0.54	1.24	26	170	NA
Lundholm, 2010	cohort study	Sweden	10132	9 yr/12 yr	medical record	question	5 stars	prepregnancy BMI	18.5 to ≤24.9(reference)				855	4561	
Lundholm, 2010	cohort study	Sweden	10132	9 yr/12 yr	medical record	question	5 stars	prepregnancy BMI	25 to ≤29.9	0.88	0.76	1.01	282	1717	
Lundholm, 2010	cohort study	Sweden	10132	9 yr/12 yr	medical record	question	5 stars	prepregnancy BMI	≥30	1.09	0.88	1.35	114	559	
Harpsøe,2013	cohort study	Denmark	38874	7 yr	self-reported and question	questionnaires	7 stars	prepregnancy BMI	<18.5	1.09	0.97	1.22	454	1204	Adjusted for sex of the child, maternal age at conception,
Harpsøe,2013	cohort study	Denmark	38874	7 yr	self-reported and question	questionnaires	7 stars	prepregnancy BMI	18.5 to <25 (reference)				7061	20221	

Harpsøe,2013	cohort study	Den mark	38874	7 yr	self-reported and question	questionnaires	7 stars	prepregnancy BMI	25 to <30	0.96	0.90	1.02	1821	5424	maternal smoking during first trimester, number of older siblings, maternal history of allergy, GWG
Harpsøe,2013	cohort study	Den mark	38874	7 yr	self-reported and question	questionnaires	7 stars	prepregnancy BMI	30 to <35	1.02	0.91	1.13	530	1489	
Harpsøe,2013	cohort study	Den mark	38874	7 yr	self-reported and question	questionnaires	7 stars	prepregnancy BMI	≥35	0.80	0.66	0.97	146	524	
Harpsøe,2013	cohort study	Den mark	38874	7 yr	self-reported and question	questionnaires	7 stars	GWG	<5 kg	0.97	0.82	1.16	194	599	Adjusted for sex of the child, maternal age at conception, maternal smoking during first trimester, number of older siblings, maternal history of allergy, prepregnancy BMI
Harpsøe,2013	cohort study	Den mark	38874	7 yr	self-reported and question	questionnaires	7 stars	GWG	5-9 kg	0.97	0.89	1.05	957	2903	
Harpsøe,2013	cohort study	Den mark	38874	7 yr	self-reported and question	questionnaires	7 stars	GWG	10-15 kg (reference)				4626	13321	
Harpsøe,2013	cohort study	Den mark	38874	7 yr	self-reported and question	questionnaires	7 stars	GWG	16-19 kg	1.00	0.94	1.06	2130	6100	
Harpsøe,2013	cohort study	Den mark	38874	7 yr	self-reported and question	questionnaires	7 stars	GWG	20-24 kg	1.00	0.94	1.08	1405	4046	
Harpsøe,2013	cohort study	Den mark	38874	7 yr	self-reported and question	questionnaires	7 stars	GWG	≥25 kg	1.06	0.97	1.17	700	1893	
Ekström,2015	cohort study	Swed en	3294	16 yr	medical record	questionnaires	7 stars	continuous BMI	5 kg/m2 increase in BMI	1.03	0.93	1.14	NA	NA	Adjusted for gender, maternal age, parental history of allergic disease, older siblings, socio-economic

															status and maternal smoking in pregnancy and/or at baseline.
El-Heis,2016	cohort study	UK	467	12 mo	medical record	questionnaire	7 stars	continuous BMI	1 kg/m ² increase in BMI	1.07	1.03	1.13	NA	NA	Adjusted for serum nicotinamide, maternal age, maternal education, smoking in pregnancy, parity, maternal eczema, infant sex, gestational age, breast feeding duration
El-Heis,2016	cohort study	UK	467	12 mo	medical record	questionnaire	7 stars	continuous BMI	1 kg/m ² increase in BMI	1.07	1.02	1.14	NA	NA	Adjusted for Serum anthranilic acid, maternal age, maternal education, smoking in pregnancy, parity, maternal

															eczema, infant sex, gestational age, breast feeding duration
Goudarzi,2018	cohort study	Japan	3296	1 yr,2 yr,4 yr,7 yr	questionnaire	questionnaires	7 stars	continuous BMI(7y)	1 kg/m2 increase in BMI	0.97	0.94	0.99	NA	NA	Adjusted for child's sex, maternal education, maternal age, maternal history of allergy, birth weight, maternal smoking history during pregnancy, comorbid allergic diseases at the same age and children's BMI at age 7.
Drucker,2019	cohort study	USA	13269	17 yr	questionnaires	question	7 stars	prepregnancy BMI	< 20.0	1.12	0.99	1.27	530	NA	Adjusted for maternall age at
Drucker,2019	cohort study	USA	13269	17 yr	questionnaires	question	7 stars	prepregnancy BMI	20-22.4(reference)				812	NA	delivery, asthma, atopic dermatitis,
Drucker,2019	cohort study	USA	13269	17 yr	questionnaires	question	7 stars	prepregnancy BMI	22.5-24.9	1.11	0.97	1.26	417	NA	race, ethnicity, smoking in

Drucker,2019	cohort study	USA	13269	17 yr	questionnaires	question	7 stars	prepregnancy BMI	25-29.9	1.02	0.86	1.20	226	NA	child's early life, household income, husband's education, US region in child's early life, mode of delivery (C-section), child's birth order, and breast feeding duration
Drucker,2019	cohort study	USA	13269	17 yr	questionnaires	question	7 stars	prepregnancy BMI	30	0.99	0.75	1.30	73	NA	
Drucker,2019	cohort study	USA	13269	17 yr	questionnaires	question	7 stars	GWG	< 15 lb	1.07	0.78	1.47	58	NA	Adjusted for maternall age at delivery, asthma, atopic dermatitis, race, ethnicity, smoking in
Drucker,2019	cohort study	USA	13269	17 yr	questionnaires	question	7 stars	GWG	15-24 lb	0.96	0.84	1.10	391	NA	
Drucker,2019	cohort study	USA	13269	17 yr	questionnaires	question	7 stars	GWG	25-34 lb (reference)				810	NA	
Drucker,2019	cohort study	USA	13269	17 yr	questionnaires	question	7 stars	GWG	34-44 lb	1.11	0.98	1.26	483	NA	child's early life, household income, husband's education, US region in child's early life, mode of delivery
Drucker,2019	cohort study	USA	13269	17 yr	questionnaires	question	7 stars	GWG	45 lb	1.23	1.05	1.43	316	NA	

															(C-section), child's birth order, and breast feeding duration
Drucker,2019	cohort study	USA	132 69	17 yr	questionnaires	question	7 stars	GWG relative to recommen dations	Under	0. 94	0. 82	1. 07	397	NA	Adjusted for maternall age at delivery, asthma, atopic dermatitis, race, ethnicity, smoking in child's early life, household income, husband's education, US region in child's early life, mode of delivery (C-section), child's birth order, and breast feeding duration
Drucker,2019	cohort study	USA	132 69	17 yr	questionnaires	question	7 stars	GWG relative to recommen dations	Meet (reference)				970	NA	
Drucker,2019	cohort study	USA	132 69	17 yr	questionnaires	question	7 stars	GWG relative to recommen dations	Over	1. 08	0. 96	1. 20	961	NA	
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregna ncy BMI(6 mo)	18.5 to ≤24.9 (reference)				8	106	NA

Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(6 mo)	25 to ≤ 29.9	1.28	0.43	3.87	6	62	
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(6 mo)	≥ 30	2.11	0.85	5.26	14	88	
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(12 mo)	18.5 to ≤ 24.9 (reference)				7	112	
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(12 mo)	25 to ≤ 29.9	1.27	0.39	4.17	5	63	
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(12 mo)	≥ 30	1.57	0.56	4.36	9	92	
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(18 mo)	18.5 to ≤ 24.9 (reference)				12	105	
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy	25 to ≤ 29.9	1.54	0.62	3.77	10	57	

								BMI(18 mo)									
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(18 mo)	≥ 30	1.19	0.51	2.79	12	88			
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(24 mo)	18.5 to ≤ 24.9 (reference)				19	85			
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(24 mo)	25 to ≤ 29.9	1.79	0.85	3.75	18	45			
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(24 mo)	≥ 30	2.43	1.26	4.68	32	59			
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(30 mo)	18.5 to ≤ 24.9 (reference)				16	87			
Castro-Rodriguez,2020	cohort study	Chile	339	30 mo	medical record	question	6 stars	prepregnancy BMI(30 mo)	25 to ≤ 29.9	1.50	0.64	3.51	11	40			

Castro-Rodriguez, 2020	cohort study	Chile	339	30 mo	medical record	questionnaire	6 stars	prepregnancy BMI (30 mo)	≥30	2.10	1.02	4.34	22	57	
Chen, 2020	cross-sectional study	China	151	13-14 yr	questionnaire (prepregnancy BMI) questionnaire and medical record (GWG)	questionnaire	6 scores	prepregnancy BMI	<18.5	1.03	0.98	1.07	NA	NA	Adjusted for maternal age at delivery, paternal age at delivery, family income, parity, maternal smoking during pregnancy, maternal alcohol intake during pregnancy, paternal smoking during pregnancy, and family history of allergic disease.
Chen, 2020	cross-sectional study	China	151	13-14 yr	questionnaire (prepregnancy BMI) questionnaire and medical record (GWG)	questionnaire	6 scores	prepregnancy BMI	18.5-22.9 (reference)				NA	NA	
Chen, 2020	cross-sectional study	China	151	13-14 yr	questionnaire (prepregnancy BMI) questionnaire and medical record (GWG)	questionnaire	6 scores	prepregnancy BMI	≥23	0.98	0.92	1.04	NA	NA	
Chen, 2020	cross-sectional study	China	151	13-14 yr	questionnaire (prepregnancy BMI) questionnaire and	questionnaire	6 scores	GWG	<10 kg	0.89	0.84	0.94	NA	NA	Adjusted for maternal age at delivery, paternal age at delivery,

					medical record(GWG)											family income, parity, maternal smoking during pregnancy, maternal alcohol intake during pregnancy, paternal smoking during pregnancy, and family history of allergic disease.
Chen,2020	cross-se ctional study	Chin a	151	3-14 45yr	questionnaire(pr epregnancy BMI) questionnair and medical record(GWG)	question naire	6 scores	GWG	10-15 kg (reference)					NA	NA	
Chen,2020	cross-se ctional study	Chin a	151	3-14 45yr	questionnaire(pr epregnancy BMI) questionnair and medical record(GWG)	question naire	6 scores	GWG	15-25 kg	1. 09	1. 04	1. 13		NA	NA	
Chen,2020	cross-se ctional study	Chin a	151	3-14 45yr	questionnaire(pr epregnancy BMI) questionnair and medical record(GWG)	question naire	6 scores	GWG	≥25 kg	1. 15	1. 07	1. 24		NA	NA	
Chen,2020	cross-se ctional study	Chin a	151	3-14 45yr	questionnaire(pr epregnancy BMI) questionnair and medical record(GWG)	question naire	6 scores	GWG relative to recommen dations	Under	0. 86	0. 82	0. 91		NA	NA	Adjusted for maternal age at delivery, paternal age at delivery, family income, parity, maternal

[illegible]

Table Study classification for Systematic Review and Meta-analysis

First author, year	maternal obesity	maternal overweight	maternal underweight	continuous BMI	GWG (<10kg)	GWG (15-25kg)	GWG (>25kg)	excessive GWG	inadequate GWG
Xu,1999									
Ushiyama,2002				√					
Moore,2004				√					
Kumar,2010	√	√							
Lundholm, 2010	√	√	√						
Harpsøe,2013	√	√	√		√	√	√		
Ekström,2015				√					
El-Heis,2016				√					
Goudarzi,2018				√					
Drucker,2019	√	√	√		√	√	√	√	√
Castro-Rodriguez,2020	√	√							
Chen,2020	√		√		√	√	√	√	√
Richards,2020	√	√	√						
total	7			5	3			2	