#### REVIEW

# Association between maternal pre-pregnancy BMI and preeclampsia: An updated systematic review and meta-analysis of cohort studies

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Abstract. Background and aim: Although several studies have previously explored the association between maternal body mass index and the risk of preeclampsia, an updated meta-analysis is necessary. This study seeks to conduct a systematic review and meta-analysis to reassess the relationship between preeclampsia and pre-pregnancy BMI, categorized into three groups—overweight, obese, and overweight & obese—and to calculate the pooled effect size (crude Odds Ratios) for each group. Methods: A comprehensive search was conducted in four electronic literature databases: PubMed, Scopus, ScienceDirect, and Google Scholar. The pooled mean effect size was calculated using a random-effects model for meta-analysis. Results: Sixteen articles were included in the meta-analysis. The pooled crude odds ratio for preeclampsia in overweight patients is 1.96 (95% CI [1.75; 2.21]), in obese patients it is 3.89 (95% CI [3.32; 4.57]), and in overweight & obese patients it is 4.19 (95% CI [3.36; 5.24]). Meta-regression did not reveal a significant association between the year of publication and the risk of preeclampsia. Conclusions: The findings confirm that higher BMI categories are associated with a significantly increased risk of preeclampsia, with the risk escalating as BMI increases. Chinese patients with lower BMI values to classify patients as overweight or obese compared to the rest of the population showed stronger associations between pre-pregnancy BMI and preeclampsia. As a result of these findings, the importance of managing weight before pregnancy is underscored, as is the importance of considering patient specific factors when assessing the risk for preeclampsia. (www.actabiomedica.it)

**Key words:** preeclampsia, obesity, overweight, body mass index, pre-pregnancy, systematic review, meta-analysis, cohort studies, pregnancy complications, maternal health

#### Introduction

According to the World Health Organization (WHO), overweight is characterized by excessive fat deposits in the body, and 2.5 billion adults aged 18 and older were overweight in 2022; obesity, on the other hand, is a chronic disease in which excessive fat deposits can impair health, and 890 million adults aged 18 and older were obese in 2022 (1). In addition to

increasing the risk of diabetes and heart disease, obesity can harm bone health and reproduction, as well as increase the risk of certain cancers (1). The quality of living is affected by obesity in a variety of ways, including impaired sleeping and moving (1). Globally, the prevalence of adult obesity has more than doubled since 1990. Overweight and obesity rates are on the rise, which not only poses significant health challenges but also poses a pressing economic challenge for

healthcare systems worldwide. Based on a cost analysis using statistical life values, the economic burden of obesity is expected to reach \$3,411.55 billion in the United States in 2024, \$1,874.87 billion in China, and \$956.78 billion in Russia (2). Furthermore, overweight and obesity in pregnant women pose a threat not only to maternal but also to infant health (3,4). For mothers, major adverse health outcomes are gestational diabetes, pregnancy-induced hypertension, preeclampsia, post-partum hemorrhage and caesarean delivery (3,4). For infants, short-term major adverse health outcomes include low birth weight, preterm birth, being small for gestational age, and stillbirth (5,6). In the long term, maternal overweight and obesity can lead to an increased risk of obesity, diabetes, and cardiovascular disease in the infant's later life (7). Similar to how the trend of overweight and obesity has more than doubled in in the last three decades, hypertensive disorders of pregnancy have also been on the uprise (8). Hypertensive disorders, including preeclampsia are a major cause of maternal death (9). Preeclampsia is a pregnancy disorder marked by placental dysfunction, causing the release of factors that damage maternal blood vessels, leading to high blood pressure, organ damage, and potential complications like fetal growth restriction or stillbirth(10). Characterized by elevated blood pressure, extremity edema, and proteinuria, preeclampsia typically manifests after 20 weeks of gestation (11). The risk of preeclampsia has been found to strongly correlate with a higher body mass index (BMI) (12). Although several studies have previously explored the association between maternal BMI and the risk of preeclampsia, an updated meta-analysis is necessary. A 2018 study by He and co-authors combined the results of 13 studies on overweight patients and 19 studies on obese patients into a meta-analysis, with no specified definition of overweight and obesity used for the study (13). An earlier meta-analysis by Poorolajal and Ensiyeh (2016) used the WHO definition of overweight and obesity (14). However, there are several key reasons to update these analyses. First, the He (2018) study used adjusted Odds Ratios (OR) from cohort studies, which may introduce inconsistencies. Second, the Poorolajal (2016) study limited the definition of overweight and obesity to WHO guidelines. Finally, since 2018, numerous new publications

from various countries have emerged, potentially altering the established association. This study seeks to conduct a systematic review and meta-analysis to reassess the relationship between preeclampsia and pre-pregnancy BMI, categorized into three groups—overweight, obese, and overweight & obese—and to calculate the pooled effect size (crude OR) for each group.

# Materials and Methods

The study protocol is registered with the PROS-PERO International prospective register of systematic reviews (15)(Reference ID: CRD42024585347). Asfendiyarov Kazakh National Medical University's institutional review board (Local Ethics Committee) that this systematic review did not meet the definition of human subject research. Thus, there was no need for a board review.

# Search strategy

The PROSPERO database was searched to identify the registration of similar studies, and no current similar studies were found. We conducted a subsequent search in four major electronic healthcare literature databases: PubMed, Scopus, ScienceDirect, and Google Scholar. The literature search was initiated on May 15, 2024, and completed on July 01, 2024. The search strategy incorporated the following keywords: pregnancy AND ("body mass index" OR BMI OR overweight OR obesity OR obese) AND preeclampsia. The depth of the search was limited to articles published from January 2018. An additional filter was applied to limit the search to publications in English.

# Eligibility criteria

Methodologically, the literature screening and synthesis adhered to the recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (16). The inclusion criteria for study selection comprised: (a) cohort studies reporting effect of pre-pregnancy overweight and obesity on preeclampsia compared

to normal weight in singleton pregnancies; (b) crude odds ratios (OR) with 95% confidence intervals (CI); (c) full-text publications in English. Exclusion criteria encompassed: (a) studies reporting pregnancy induced hypertension or combined risk of preeclampsia/eclampsia and other conditions; (b) studies on twin pregnancies; (c) studies reporting only adjusted ORs or risk ratios; (d) studies where the reference group is not normal weight; (e) editorials, commentaries, and reviews.

## Selection of studies and data extraction

After identifying the publications, we conducted deduplication and performed initial screening based on titles and abstracts, followed by a thorough evaluation of eligibility through full-text examination. During this process, publications were excluded according to predetermined inclusion and exclusion criteria. Adhering to the PRISMA guidelines, two independent authors then extracted relevant data from the full-text articles using a standardized form. The extracted information encompassed details such as the name of the first author, publication year, country, study period, when BMI was evaluated, number of total patients in the study, BMI criteria, number of overweight, obese and overweight and obese patients, crude OR of preeclampsia, 95% CI for the crude OR of preeclampsia, adjusted OR with 95% CI of preeclampsia, and controlled factors.

# Risk of bias

The risk of bias (quality) of the included studies was assessed using the Critical Appraisal Skills Programme (CASP) Checklist for Cohort Studies (17). The checklist consisted of twelve questions in three major domains: validity of the study results, what the results are, and the value of the study results. Two questions were not assigned a score, and two questions had two parts each, with each part receiving a full score. Each criterion was rated as 'yes' (scored as 1) when adequately described, 'no' (scored as 0) when absent, and 'can't tell' (scored as 0.5) when unclear or incomplete. Total scores ranged from 0 to 12, with a score of at least 7 indicating satisfactory quality.

## Statistical analysis

The pooled mean effect size (crude OR), along with 95% confidence intervals (95% CI), was calculated using a random-effects model for meta-analysis in RStudio software (18). Heterogeneity across studies was assessed using the I2-statistic. When high heterogeneity was observed, a subgroup analysis based on BMI values was conducted to explore its sources. Influence analysis was carried out to identify any studies that significantly influenced the pooled prevalence estimates. Additionally, meta-regression analyses were performed to evaluate the effect of the year of publication on the effect size. Publication bias was assessed through visual inspection of a funnel plot and statistical analysis using Egger's test. The funnel plot displays the log of the odds ratios on the x-axis and the standard error on the y-axis. The distribution of the estimated effect sizes was plotted according to significance levels on the funnel plot, with dark grey and black regions indicating 0.95 and 0.99 significance levels. The presence of publication bias is determined by examining the proportion of estimated effect sizes falling within the non-significant areas of the grey and white regions.

#### Results

A comprehensive search across PubMed, Scopus, ScienceDirect, and Google Scholar databases resulted in 854 records. After initial screening, 788 non-duplicative records remained, of which 108 full-text articles were evaluated. Sixteen articles that reported only adjusted ORs of preeclampsia in overweight and obese patients compared to those of normal weight were excluded from this analysis. Additionally, six studies that seemed to meet the inclusion criteria were excluded because their reference group consisted of non-obese patients rather than those of normal weight (19–24). Ultimately, sixteen articles met the criteria for inclusion in the systematic review. The study selection process is illustrated in Figure 1 (16).

# Description of the included studies

The study descriptions and patient characteristics are presented in Table 1. Only studies published

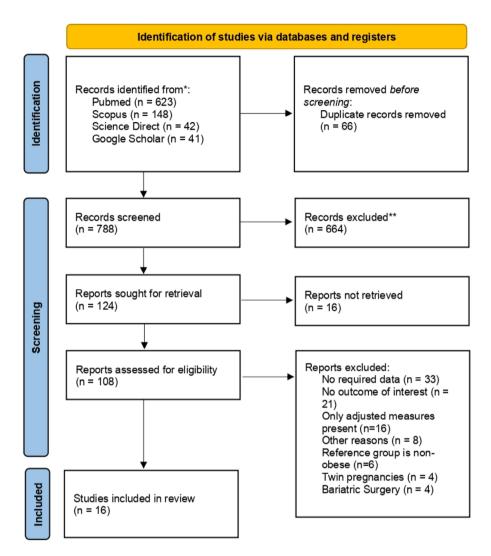


Figure 1. PRISMA flow chart of study selection (16).

between 2018 and 2024 were included in the present analysis, according to the exclusion and inclusion criteria. One study combined patients from European, North American, and Australian cohorts. The majority of the studies were from South Asia: three from Taiwan, three from China, and three from Indonesia. Three studies were conducted in Europe (Norway, Spain, and France), one in the Middle East (Iran), and one in Africa (Tanzania). A total of 809,773 patients were included across fifteen studies (mean sample size = 53,984.87 patients, range = 70 to 382,618 patients). Ten studies presented both adjusted and unadjusted ORs of preeclampsia in overweight and obese patients.

Twelve studies, with sixteen groups, reported the crude ORs of preeclampsia in overweight patients with a BMI of 24-28 (two studies) and ten studies, with fourteen groups, in patients with a BMI of 25-29.9, which corresponds to the WHO definition of overweight. The Chaemsaithong (2019) study presented three groups: a) total, b) preterm, and c) term preeclampsia (25). The Sole (2021) study also presented three groups: a) early, b) intermediate, and c) late preeclampsia (26). Twelve studies, with nineteen groups, reported the crude ORs of preeclampsia in obese patients with a BMI of 28 and above (two studies), and ten studies, with fourteen groups, in patients with a BMI of 30 and above, which

Table 1. Summary of Included Articles and Sources.

#	Study	Country	Study period	Cohort	BMI 25-29.9	BM	I≥30
1	Mohammadi, 2018 (31)	Iran	6 to 21 July 2015	4397	1434	2	472
2	Mrema, 2018 (32)	Tanzania	July 2000-May 2013	17738	4258	12	294
3	Chaemsaithong, 2019 (25)	China	2010 - 2016	67248	8139	17	773
4	Santos, 2019 (27)	Europe, North America & Australia	1989 onward	265270	45180	187	797
5	Chen, 2020 (33)	Taiwan	January 2005 - December 2005	19052	1524	:	344
6	Liang, 2020 (34)	Taiwan	January 2014 - May 2015	2210	305		91
7	Rafida, 2021 (35)	Indonesia	January 2016 - December 2019	210	113		60
8	Sole, 2021 (26)	Norway	1999 and 2014	382618	18891	99	931
9	Gonzalez-Plaza, 2022 (36)	Spain	January 2015 - December 2016	5447	1032	2	458
10	Lautredou, 2022 (37)	France	April 2013 - May 2015	3162	583	4	400
Oth	er BMI classification						
#	Study	Country	Study period	Cohort	BMI≥23 & BMI ≥24	BMI 24-28	BMI ≥28
1	Ermamilia, 2020 (28)	Indonesia	May to August 2017	70	35		
2	Suryowati, 2023 (30)	Indonesia	March 2020 - March 2022	128	113		
3	Chuang, 2024 (29)	Taiwan	2011 - 2019	8146	2319		
4	Zhang, 2022 (38)	China	October 2018 - April 2020	1546		238	105
5	Zhang, 2022 (39)	China	March 2013 - December 2020	32531		3881	720

Abbreviations: BMI - body mass index; WHO - World Health Organization.

corresponds to the WHO definition of overweight. One study also presented crude ORs of preeclampsia in three obesity groups: group 1 with a BMI of 30-35, group 2 with a BMI of 35-40, and group 3 with a BMI of 40 and above (27). Three studies, with four groups, reported the crude ORs of preeclampsia in overweight and obese patients with a BMI above 23 (one study) (28) and two studies with three groups with a BMI of 24 and above (29,30). The Chuang (2024) study presented two groups: a) preeclampsia, and b) severe preeclampsia (29).

The risk of bias assessment

The risk of bias assessment results is presented in Table 2. All of the studies had a low risk of bias with a CASP score of 10.5 and above.

Association between pre-pregnancy excessive BMI and preeclampsia

Below is a summary of the preeclampsia risk in three groups of patients: overweight, obese, and

**Table 2.** CASP risk of bias assessment.

	pag	Acceptable	Exposure	Outcome	Confounding	Confounding			Believe		Ė		
Author, year	issue	recruitment	measure	measure	identihed	measured	tollow up	tollow up	hnding	Applicability	Fit	Implications	Score
Mohammadi, 2018 (31)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	11.5
Mrema, 2018 (32)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	11.5
Chaemsaithong, 2019 (25)	Yes	Yes	Yes	Yes	Yes	No	Yes	Can't tell	Yes	Yes	Yes	Yes	10.5
Santos, 2019 (27)	Yes	Yes	Yes	Yes	Yes	No	Yes	Can't tell	Yes	Yes	Yes	Yes	10.5
Chen, 2020 (33)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	11.5
Ermamilia, 2020 (28)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	11.5
Liang, 2020 (34)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	11.5
Rafida, 2021 (35)	Yes	Yes	Yes	Yes	Yes	No	Yes	Can't tell	Yes	Yes	Yes	Yes	10.5
Sole, 2021 (26)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	11.5
Gonzalez-Plaza, 2022 (36)	Yes	Yes	Yes	Yes	Yes	No	Yes	Can't tell	Yes	Yes	Yes	Yes	10.5
Lautredou, 2022 (37)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	11.5
Jing Zhang, 2022 (38)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	11.5
Senmao Zhang, 2022 (39)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	11.5
Suryowati, 2023 (30)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	11.5
Chuang, 2024 (29)	Yes	Yes	Yes	Yes	Yes	No	Yes	Can't tell	Yes	Yes	Yes	Yes	10.5

Abbreviations: CASP: Critical Appraisal Skills Programme.

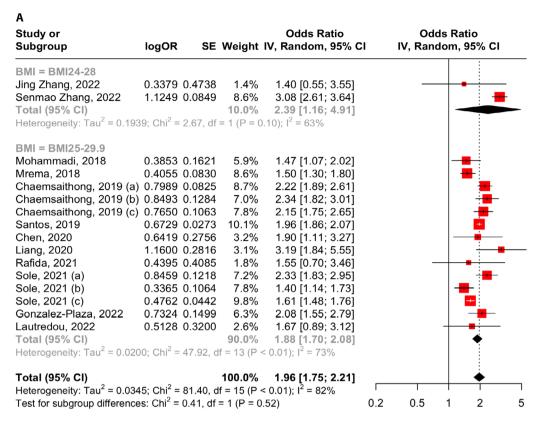


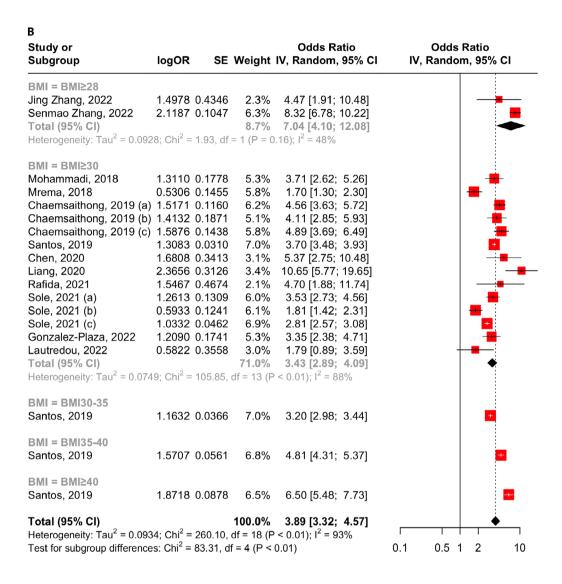
Figure 2. Meta-Analysis of Crude Association of BMI with Preeclampsia Risk in: A) Overweight Patients; B) Obese Patients; and C) Combined Overweight & Obese Patients.

Abbreviations: CI: confidence interval; SE: standard error.

Chaemsaithong, 2019 (a): total preeclampsia; Chaemsaithong, 2019 (b): preterm preeclampsia; Chaemsaithong, 2019 (c): term preeclampsia. Sole, 2021 (a): early preeclampsia; Sole, 2021 (b): intermediate preeclampsia; Sole, 2021 (c): late preeclampsia. Chuang, 2024 (a): preeclampsia; Chuang, 2024 (b): severe preeclampsia.

overweight & obese patients. Studies presenting the crude ORs of preeclampsia in overweight patients, defined as either BMI 24-28 or BMI 25-29.9, were grouped together (Figure 2, A). The results from the random effects model indicate that the pooled OR of preeclampsia in overweight patients is 1.96 (95% CI [1.75; 2.21]). A test for heterogeneity revealed substantial heterogeneity (I<sup>2</sup>=82%, Q(df=15)=81.40, p-value<0.01). To explore sources of this heterogeneity, a subgroup analysis was conducted. The pooled OR of preeclampsia in overweight patients with BMI 24-28 from the random effects model is 2.39 (95% CI [1.16; 4.91]), with non-significant heterogeneity ( $I^2=63\%$ , Q(df=1)=2.67, p-value=0.10). For those with BMI 25-29.9, the pooled OR is 1.88 (95% CI [1.70; 2.08]), with modest heterogeneity ( $I^2=73\%$ ,

Q(df=13)=47.92, p-value<0.01). Studies presenting crude ORs of preeclampsia in obese patients, defined as BMI above 28, were grouped together (Figure 2, B). The random effects model revealed a pooled OR of 3.89 (95% CI [3.32; 4.57]). Substantial heterogeneity was observed (I<sup>2</sup>=93%, Q(df=18)=260.10, p-value<0.01). Subgroup analysis indicated that the pooled OR of preeclampsia in patients with BMI 28 and above is 7.04 (95% CI [4.10; 12.08]), with low heterogeneity (I<sup>2</sup>=48%, Q(df=1)=1.93, p-value=0.16). For those with BMI 30 and above, the pooled OR is 3.43 (95% CI [2.89; 4.09]), with high heterogeneity  $(I^2=88\%, Q(df=13)=105.85, p-value<0.01)$ . Further analysis showed the pooled OR of preeclampsia in patients with BMI 30–35 is 3.20 (95% CI [2.98; 3.44]), BMI 35–40 is 4.81 (95% CI [4.31; 5.37]), and BMI 40



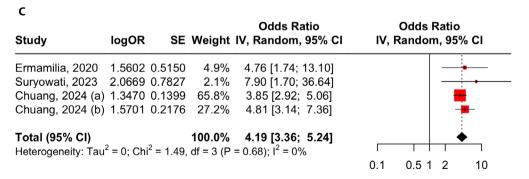
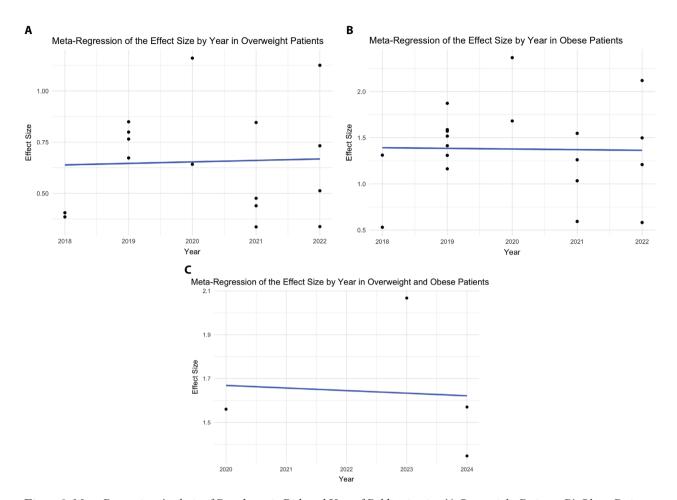


Figure 2. (continued)



**Figure 3.** Meta-Regression Analysis of Preeclampsia Risk and Year of Publication in: A) Overweight Patients; B) Obese Patients; and C) Combined Overweight & Obese Patients.

and above is 6.50 (95% CI [5.48; 7.73]). Finally, studies that presented crude ORs of preeclampsia in overweight & obese patients, defined as either BMI above 23 or BMI above 24, were grouped together (Figure 2, C). The random effects model showed a pooled OR of 4.19 (95% CI [3.36; 5.24]). No heterogeneity was detected (I²=0%, Q(df=3)=1.49, p-value=0.68).

## Meta-Regression results

A meta-regression analysis was conducted to evaluate the influence of the year of publication on the risk of preeclampsia in three patient groups: overweight patients (Figure 3, A), obese patients (Figure 3, B), and combined overweight and obese patients

(Figure 3, C). The analysis did not reveal a statistically significant association between the year of publication and the risk of preeclampsia.

## Influence analysis

An influence analysis was conducted to determine which studies most affected the pooled estimate. In the overweight patients' group, the pooled OR was most influenced by study #2, the Senmao Zhang, 2022 study (Figure 4, A) (39). In the obese patients' group, no study had an extreme influence on the pooled estimate result (Figure 4, B). In the overweight & obese patients' group, the pooled OR was most influenced by study #3, the Chuang, 2024 (a) study (Figure 4, C) (29).

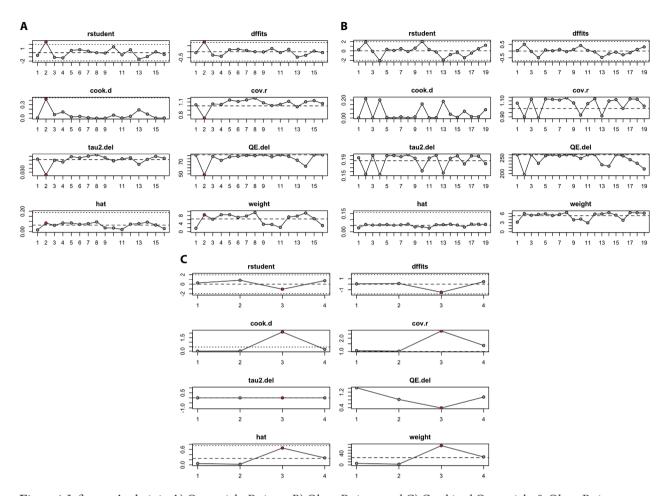


Figure 4. Influence Analysis in A) Overweight Patients; B) Obese Patients; and C) Combined Overweight & Obese Patients.

### Publication bias assessment

Upon visual inspection of the funnel plots presented in Figure 5 (A, B, C), we observed that, in all three patient groups examined, the majority of the estimated effect sizes fell within the p<0.01 significance level in the black-shaded region, indicating no evidence of publication bias. These findings were further confirmed by non-significant results from Egger's test for publication bias in all three groups (p>0.05).

# Adjusted odds ratios presented in included studies

Table 3 summarizes the adjusted ORs for preeclampsia among overweight, obese and overweight & obese women. All the studies adjusted the ORs of preeclampsia for different demographic, medical and social factors.

# Discussion

This systematic review and meta-analysis aimed to reassess the relationship between preeclampsia and prepregnancy body mass index, stratifying pre-pregnancy BMI according to three groups (overweight, obese, and overweight & obese) and calculating the pooled effect size (crude OR) for each group separately. In the present meta-analysis, 16 studies were included, representing a broad geographic range, including Europe, South Asia, the Middle East, Africa, Australia, and North America. The pooled OR of preeclampsia in overweight patients is 1.96 (95% CI [1.75; 2.21]); in obese patients, it is 3.89 (95% CI [3.32; 4.57]); and in overweight & obese patients, it is 4.19 (95% CI [3.36; 5.24]). Our results clearly demonstrate an association between pre-pregnancy BMI and the development of preeclampsia in singleton pregnancies. Findings of the

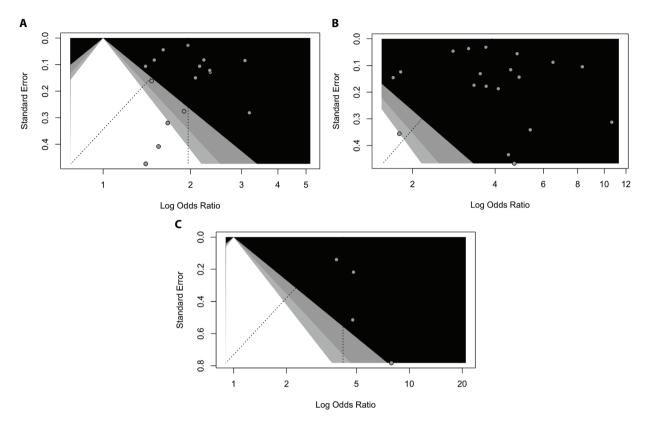


Figure 5. Publication Bias Assessment in: A) Overweight Patients; B) Obese Patients; and C) Combined Overweight & Obese Patients.

present analysis align with previous studies in terms of the direction of the association. However, the effect size in our analysis is higher than in the earlier metaanalysis by He and co-authors, which reported a pooled adjusted OR of 1.71 (95% CI [1.52; 1.91]) for overweight patients and a pooled adjusted OR of 2.48 (95% CI [2.05; 2.90]) for obese patients (13). This discrepancy can be attributed to the different measures used in the two meta-analyses. We opted to combine crude ORs, as adjustments in the included studies were made for various factors, introducing potential heterogeneity to the adjusted ORs (40). Another meta-analysis by Rahman and co-authors (2015) also noted that the association between preeclampsia and maternal BMI is influenced by confounding adjustments (41). A study by Poorolajal and Ensiyeh performed a meta-analysis to investigate the association between preeclampsia and pre-pregnancy BMI, using the WHO guidelines to define overweight and obesity (overweight: 25–29.9 kg/m<sup>2</sup>; obese: ≥30 kg/m<sup>2</sup>) (14). This criterion potentially limited the number of studies that could

be included in their analysis. In our study, we did not use pre-specified criteria for overweight or obesity but instead used the definitions proposed by the authors of the included studies. This approach resulted in two BMI groups within the overweight category: a BMI of 24 to 28, used specifically for the Chinese population (42), and the WHO classification of overweight (BMI of 25 to 29.9) (43). In the Chinese population, even the lower cutoff point for overweight classification showed a stronger association between preeclampsia and overweight than in other populations, with a pooled crude OR of 2.39 (95% CI [1.16; 4.91]) compared to a pooled OR of 1.88 (95% CI [1.70; 2.08]), respectively. Similarly, in the obese patient group, there were two main BMI groups: BMI ≥28 for the Chinese population and BMI ≥30 for the rest of the patients, with a stronger association and absence of heterogeneity in the Chinese population, yielding a pooled crude OR of 7.04 (95% CI [4.10; 12.08]) compared to 3.43 (95% CI [2.89; 4.09]), respectively. Santos and co-authors (2019) also demonstrated an association between

Table 3. Summary of Adjusted Association between BMI and Preeclampsia Risk.

Study	Adjustment	Adjusted OR (95% CI)		
Overweight, BMI 24-28				
Jing Zhang, 2022 (38)	All analyses were adjusted for age and conception method	1.340 (0.523 - 3.436)		
Senmao Zhang, 2022 (39)	Adjusted for maternal age, educational level, income (RMB), residence, family history of hypertension, drinking in early pregnancy, gestational diabetes mellitus	2.71 (2.29 - 3.21)		
Overweight, BMI 25 – 29.9				
Mohammadi, 2018 (31)	Adjusted for mother's age and parity	1.47 (1.06 - 2.02)		
Mrema, 2018 (32)	Adjusted according to risk factors	1.4 (1.2 - 1.8)		
Chen, 2020 (33)	Adjusted for maternal age, maternal immigration status, parity, maternal smoking during pregnancy, family income, maternal educational status, infant sex, living area	1.87 (1.08 - 3.26)		
Sole, 2021 (26)	Adjusted for maternal age, country of birth, education, 1st-trimester smoking, diabetes and chronic hypertension	2.22 (1.73 - 2.84) (early preeclampsia) 1.25 (1.01 - 1.55) (intermediate preeclampsia) 1.52 (1.39 - 1.66) (late preeclampsia)		
Obese, BMI≥28				
Jing Zhang, 2022 (38)	All analyses were adjusted for age and conception method	3.512 (1.408 - 8.762)		
Senmao Zhang, 2022 (39)	Adjusted for maternal age, educational level, income (RMB), residence, family history of hypertension, drinking in early pregnancy, gestational diabetes mellitus	7.17 (5.82 - 8.84)		
Obese, BMI≥30				
Mohammadi, 2018 (31)	Adjusted for mother's age and parity	3.67 (2.57 - 5.24)		
Mrema, 2018 (32)	Adjusted according to risk factors	1.8 (1.3 - 2.4)		
Chen, 2020 (33)	Adjusted for maternal age, maternal immigration status, parity, maternal smoking during pregnancy, family income, maternal educational status, infant sex, living area	5.01 (2.53 - 9.93)		
Liang, 2020 (34)	Adjustment for age and each variable based on model selection	3.65 (1.41 - 9.44)		
Sole, 2021 (26)	Adjusted for maternal age, country of birth, education, 1st-trimester smoking, diabetes and chronic hypertension	3.20 (2.44 - 4.21) (early preeclampsia) 1.40 (1.08 - 1.82) (intermediate preeclampsia) 2.54 (2.31 - 2.79) (late preeclampsia)		
Lautredou, 2022 (37)	Confounding factors included in the multivariable analysis were. age, parity, geographical origin, tobacco use, gestational age, preexisting diabetes and preexisting chronic hypertension	1.55 (0.63 - 3.80)		
Overweight & Obese				
Ermamilia, 2020 (28)	Adjusted for age, hypertension history, GWG/BMI	3.28 (1.04 - 10.4)		
Suryowati, 2023 (30)	Adjusted for age, parity status, previous history of preeclampsia, family history of preeclampsia, and chronic hypertension	8.267 (1.386 - 49.304)		

different obesity groups, classifying patients into three categories: obesity class I with BMI of 30-35, obesity class II with BMI of 35-40, and obesity class III with BMI of above 40, for cohorts from Europe, North America, and Australia, where higher BMI was associated with higher odds of developing preeclampsia (27). When considering the association between maternal BMI and preeclampsia, it is crucial to note that these patients also face a higher risk of gestational diabetes, pregnancy-induced hypertension, cesarean delivery, postpartum hemorrhage, and other maternal complications (3,4,41,44-46). Moreover, preeclampsia is a multifactorial condition influenced not only by BMI but also by a variety of factors including maternal age, parity, and chronic medical conditions (47,48). Effective management of excessive body weight and other risk factors, including the use of bariatric surgery in obese patients, has been shown to improve maternal and neonatal outcomes (49-52). While the analysis of such outcomes is outside the scope of the present study, investigating the association between excessive body weight and preeclampsia in patients after bariatric surgery could be a focus of future research. Limitations of the present analysis: the results presented here are based on crude ORs from cohort studies, which are generally associated with inherent biases. While the use of crude ORs allows for straightforward comparisons across studies, it does not account for the influence of important risk factors, potentially leading to the overestimation or underestimation of the true association between BMI and preeclampsia. Additionally, we must acknowledge the presence of high heterogeneity in the analysis results, particularly within the obese patient group. Although subgroup analysis reduced the heterogeneity, it did not eliminate it, indicating that other potential confounders may not have been accounted for. In conclusion, present meta-analysis shows a clear link between pre-pregnancy excessive body weight and the odds of getting preeclampsia in overweight, obese and overweight & obese women compared to normal weight women. The findings confirm that higher BMI categories are associated with a significantly increased risk of preeclampsia, with the risk escalating as BMI increases. Chinese patients with lower BMI values to classify patients as overweight or obese compared to

the rest of the population showed stronger associations between pre-pregnancy BMI and preeclampsia. As a result of these findings, the importance of managing weight before pregnancy is underscored, as is the importance of considering patient specific factors when assessing the risk for preeclampsia. However, given the limitations related to study heterogeneity, and reliance on crude ORs, further research is needed to refine these associations and explore the underlying mechanisms. Future studies should also consider the long-term impacts of maternal BMI on both maternal and fetal health. By addressing these gaps, we can develop more effective interventions to mitigate the risk of preeclampsia and improve maternal health globally.

Acknowledgements: None.

**Funding:** This research received no specific grant from any funding agency.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Author Contribution: AM: Conceptualization, Methodology, Investigation, Formal Analysis, Writing – Original /draft preparation. BB: Conceptualization, Resources, Software, Investigation, Data curation, Supervision, Writing – Review and Editing. VL: Investigation; Validation, Writing – Original/draft preparation. IZ: Writing – Original /draft preparation, Supervision, Project Administration: ND: Investigation, Resources, Software, Writing – Review and Editing. TN: Methodology, Writing – Original / draft preparation. GB: Writing – Original /draft preparation, Writing – Review and Editing.

**Availability of Data:** Data used for the analysis in this study is available from the corresponding author upon reasonable request.

**Study Registration:** The study protocol has been registered with PROSPERO database (ID: CRD42024585347).

#### References

- World Health Organization. Obesity and overweight. 2024. Available from: https://www.who.int/news-room/fact -sheets/detail/obesity-and-overweight [accessed 2024 Aug 3].
- Sweis NJ. The economic burden of obesity in 2024: a cost analysis using the value of a statistical life. Crit Public Health. 2024 Dec 31;34(1):1–13. doi: 10.1080/09581596.2024.2333407
- 3. Ovesen P, Rasmussen S, Kesmodel U. Effect of prepregnancy maternal overweight and obesity on pregnancy outcome. Obstet Gynecol. 2011;118(2):305–12. doi: 10.1097/aog.0b013e3182245d49
- Athukorala C, Rumbold AR, Willson KJ, Crowther CA. The risk of adverse pregnancy outcomes in women who are overweight or obese. BMC Pregnancy Childbirth. 2010 Sep 17;10(1):1–8. doi: 10.1186/1471-2393-10-56
- Upadhyay S, Biccha RP, Sherpa MT, Shrestha R, Panta PP, Upadhyay S. Association between maternal body mass index and the birth weight of neonates. Nepal Med Coll J. 2011;13(1):42–52.
- Vasudevan C, Renfrew M, McGuire W. Fetal and perinatal consequences of maternal obesity. Arch Dis Child Fetal Neonatal Ed. 2011 Sep;96(5):F378–82. doi: 10.1136/adc.2009.170928
- Godfrey KM, Reynolds RM, Prescott SL, et al. Influence of maternal obesity on the long-term health of off-spring. Lancet Diabetes Endocrinol. 2017 Jan;5(1):53–64. doi: 10.1016/s2213-8587(16)30107-3
- Bicocca MJ, Mendez-Figueroa H, Chauhan SP, Sibai BM. Maternal obesity and the risk of early-onset and late-onset hypertensive disorders of pregnancy. Obstet Gynecol. 2020 Jul;136(1):118–27. doi: 10.1097/aog.00000000000003901
- Lee R, Brandt JS, Joseph KS, Ananth CV. Pregnancyassociated mortality due to cardiovascular disease: impact of hypertensive disorders of pregnancy. Paediatr Perinat Epidemiol. 2024 Mar;38(3):204–15. doi: 10.1111/ppe.13055
- Chappell LC, Cluver CA, Kingdom J, Tong S. Pre-eclampsia.
  Lancet. 2021 Jul 24;398(10297):341–54. doi: 10.1016/s0140-6736(20)32335-7
- 11. Mammaro A, Carrara S, Cavaliere A, et al. Hypertensive disorders of pregnancy. J Prenat Med. 2009;3(1):1–5.
- 12. Bodnar LM, Ness RB, Markovic N, Roberts JM. The risk of preeclampsia rises with increasing prepregnancy body mass index. Ann Epidemiol. 2005 Aug;15(7):475–82. doi: 10.1016/j.annepidem.2004.12.008
- 13. He XJ, Dai RX, Hu CL. Maternal prepregnancy overweight and obesity and the risk of preeclampsia: a meta-analysis of cohort studies. Obes Res Clin Pract. 2020 Jan;14(1):27–33. doi: 10.1016/j.orcp.2020.01.004
- 14. Poorolajal J, Jenabi E. The association between body mass index and preeclampsia: a meta-analysis. J Matern Fetal Neonatal Med. 2016 Nov;29(22):3670–6. doi: 10.3109/14767 058.2016.1140738
- 15. National Institute for Health and Care Research. PROS-PERO: international prospective register of systematic reviews. 2024. Available from: https://www.crd.york.ac.uk/prospero/[accessed 2024 Mar 27].

- 16. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi: 10.1136/bmj.n71
- 17. Critical Appraisal Skills Programme. CASP checklist for cohort studies. Oxford: CASP UK; 2017. Available from: https://casp-uk.net/casp-tools-checklists/[accessed 2024 May 20].
- 18. Posit team. RStudio: integrated development environment for R. Boston: Posit Software, PBC; 2023. Available from: http://www.posit.co/ [accessed 2024 Jan 21].
- 19. Simanjuntak J, Priyanto E, Zulvayanti Z. Relationship between age, parity and body mass index in pregnant women with the incidence of preeclampsia at Prof. Dr. Margono Soekardjo Hospital Purwokerto. Indones J Obstet Gynecol Sci. 2024 Jul;7(2):169–75.
- 20. Addicott K, Nudelman M, Putty K, et al. Adverse perinatal outcomes associated with increasing maternal obesity. Am J Perinatol. 2024;41(9):1275–81. doi: 10.1055/a-2107-1585
- 21. Robillard PY. Obesity class I and II and IOM 2009 gestational weight gain recommendations 5–9 kg: an audit on 10,000 term singleton deliveries. J Matern Fetal Neonatal Med. 2023;36(1):2184222–32. doi: 10.1080/14767058.2023 .2184222
- 22. Martin-Alonso R, Prieto P, Fernández-Buhigas I, et al. Association between perinatal outcomes and maternal risk factors: a cohort study. Medicina (B Aires). 2024;60(7): 1071–81. doi: 10.3390/medicina60071071
- 23. McCall SJ, Li Z, Kurinczuk JJ, Sullivan E, Knight M. Maternal and perinatal outcomes in pregnant women with BMI > 50: an international collaborative study. PLoS One. 2019;14(2):e0211278. doi: 10.1371/journal.pone.0211278
- 24. Peeva M, Badeghiesh A, Baghlaf H, Dahan MH. Association between obesity in women with polycystic ovary syndrome and adverse obstetric outcomes. Reprod Biomed Online. 2022;45(1):159–67. doi: 10.1016/j.rbmo.2022.02.007
- 25. Chaemsaithong P, Leung TY, Sahota D, et al. Body mass index at 11–13 weeks' gestation and pregnancy complications in a Southern Chinese population: a retrospective cohort study. J Matern Fetal Neonatal Med. 2019 Jun;32(12): 2056–68. doi: 10.1080/14767058.2018.1424824
- 26. Sole KB, Staff AC, Laine K. Maternal diseases and risk of hypertensive disorders of pregnancy across gestational age groups. Pregnancy Hypertens. 2021 Aug;25:25–33. doi: 10.1016/j.preghy.2021.05.004
- 27. Santos S, Voerman E, Amiano P, et al. Impact of maternal body mass index and gestational weight gain on pregnancy complications: an individual participant data meta-analysis of European, North American and Australian cohorts. BJOG. 2019 Jul;126(8):984–95. doi: 10.1111/1471-0528.15661
- 28. Ermamilia A, Yonika L, Aulia B, Ganap EP. High prepregnancy body mass index and excessive gestational weight gain as obesity-related risk factors of preeclampsia. Top Clin Nutr. 2020 Oct;35(4):299–308. doi: 10.1097/tin.00000000 00000225
- 29. Chuang FC, Huang HY, Chen YH, Huang JP. Optimal gestational weight gain in Taiwan: a retrospective cohort study. Taiwan J Obstet Gynecol. 2024 Mar;63(2):220–4. doi: 10.1016/j.tjog.2024.01.034

30. Suryowati T, Sirait BI, Zabrina L. Risk factors of body mass index and hypertension on preeclampsia during the COVID-19 pandemic. J Complement Altern Med Res. 2023 Aug;23(3):36–50. doi: 10.9734/jocamr/2023/v23i3479

- 31. Mohammadi M, Maroufizadeh S, Omani-Samani R, Almasi-Hashiani A, Amini P. The effect of prepregnancy body mass index on birth weight, preterm birth, cesarean section, and preeclampsia in pregnant women. J Matern Fetal Neonatal Med. 2019 Nov;32(22):3818–23. doi: 10.1080/14767058.2018.1473366
- 32. Mrema D, Lie RT, Østbye T, Mahande MJ, Daltveit AK. The association between pre pregnancy body mass index and risk of preeclampsia: a registry based study from Tanzania. BMC Pregnancy Childbirth. 2018 Feb;18(1):1–9. doi: 10.1186/s12884-018-1687-3
- 33. Chen CN, Chen HS, Hsu HC. Maternal prepregnancy body mass index, gestational weight gain, and risk of adverse perinatal outcomes in Taiwan: a population-based birth cohort study. Int J Environ Res Public Health. 2020 Feb;17(4):1–12. doi: 10.3390/ijerph17041221
- 34. Liang CC, Chao M, Chang SD, Chiu SYH. Impact of prepregnancy body mass index on pregnancy outcomes, incidence of urinary incontinence and quality of life during pregnancy: an observational cohort study. Biomed J. 2020 Dec;43(6):476–83. doi: 10.1016/j.bj.2019.11.001
- 35. Rafida M, Mochtar NM, Artiningtyas ND, Anas M. Relationship of age, body mass index, and gravida in pregnant women with preeclampsia in Muhammadiyah Hospital Surabaya. Proceedings of the 4th International Conference on Sustainable Innovation 2020—Health Science and Nursing (ICoSIHSN 2020). 2021 Jan;33:37–42. doi: 10.2991/ahsr.k. .210115.008
- 36. González-Plaza E, Bellart J, Martínez-Verdú MÁ, et al. Pre-pregnancy overweight and obesity prevalence and relation to maternal and perinatal outcomes. Enferm Clin (Engl Ed). 2022 Jun;32:S23–30. doi: 10.1016/j.enfcle.2021.04.006
- 37. Lautredou M, Pan-Petesch B, Dupré PF, et al. Excessive gestational weight gain is an independent risk factor for gestational diabetes mellitus in singleton pregnancies: results from a French cohort study. Eur J Obstet Gynecol Reprod Biol. 2022 Aug;275:31–6. doi: 10.1016/j.ejogrb.2022.06.009
- Zhang J, An W, Lin L. The association of prepregnancy body mass index with pregnancy outcomes in Chinese women. J Diabetes Res. 2022;2022:8946971. doi: 10.1155/2022 /8946971
- 39. Zhang S, Qiu X, Qin J, et al. Effects of maternal prepregnancy BMI and gestational weight gain on the development of preeclampsia and its phenotypes: a prospective cohort study in China. J Clin Med. 2022 Sep;11(19):5521–31. doi: 10.3390/jcm11195521
- 40. Voils CI, Crandell JL, Chang Y, Leeman J, Sandelowski M. Combining adjusted and unadjusted findings in mixed research synthesis. J Eval Clin Pract. 2011 Jun;17(3):429–34. doi: 10.1111/j.1365-2753.2010.01444.x
- 41. Rahman MM, Abe SK, Kanda M, et al. Maternal body mass index and risk of birth and maternal health outcomes

- in low- and middle-income countries: a systematic review and meta-analysis. Obes Rev. 2015 Sep;16(9):758–70. doi: 10.1111/obr.12293
- 42. Chen C, Lu FC. The guidelines for prevention and control of overweight and obesity in Chinese adults. Biomed Environ Sci. 2004;17(Suppl):1–36.
- 43. World Health Organization. A healthy lifestyle: WHO recommendations. 2010. Available from: https://www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle---who-recommendations [accessed 2024 Aug 2].
- 44. Yao D, Chang Q, Wu QJ, et al. Relationship between maternal central obesity and the risk of gestational diabetes mellitus: a systematic review and meta-analysis of cohort studies. J Diabetes Res. 2020;2020:6303820. doi: 10.1155/2020/6303820
- 45. Chu SY, Kim SY, Schmid CH, et al. Maternal obesity and risk of cesarean delivery: a meta-analysis. Obes Rev. 2007 Sep;8(5):385–94. doi: 10.1111/j.1467-789x.2007.00397.x
- 46. Habibi N, Mousa A, Tay CT, et al. Maternal metabolic factors and the association with gestational diabetes: a systematic review and meta-analysis. Diabetes Metab Res Rev. 2022 Jul;38(5):e3532. doi: 10.1002/dmrr.3532
- 47. English FA, Kenny LC, McCarthy FP. Risk factors and effective management of preeclampsia. Integr Blood Press Control. 2015 Mar;8:7–12. doi: 10.2147/ibpc.s50641
- 48. Fox R, Kitt J, Leeson P, Aye CYL, Lewandowski AJ. Preeclampsia: risk factors, diagnosis, management, and the cardiovascular impact on the offspring. J Clin Med. 2019 Oct;8(10):1625. doi: 10.3390/jcm8101625
- 49. Boller MJ, Xu F, Lee C, Sridhar S, Greenberg MB, Hedderson MM. Perinatal outcomes after bariatric surgery compared with a matched control group. Obstet Gynecol. 2023 Mar;141(3):583–91. doi: 10.1097/aog.00000000000005088
- Moshkalova G, Karibayeva I, Kurmanova A, et al. Endometrial thickness and live birth rates after IVF: a systematic review. Acta Biomed. 2023;94(3):1–10. doi: 10.23750/abm.v94i3 .14437
- 51. Roos N, Neovius M, Cnattingius S, et al. Perinatal outcomes after bariatric surgery: nationwide population based matched cohort study. BMJ. 2013 Nov;347:f6360. doi: 10.1136/bmj.f6460
- 52. Getahun D, Fassett MJ, Jacobsen SJ, et al. Perinatal outcomes after bariatric surgery. Am J Obstet Gynecol. 2022 Jan;226(1):121.e1–121.e16. doi: 10.1136/bmj.f6460

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Received: 9 September 2024

Accepted: 15 October 2024

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