Maternal Eating Disorders and Adverse Birth Outcomes: A Systematic Review and Meta-Analysis

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ABSTRACT

Previous systematic reviews have reported on the relationship between eating disorders (EDs) and birth outcomes, but there are no existing meta-analyses on this topic. This systematic review and meta-analysis examines the association between lifetime maternal EDs, including anorexia nervosa (AN), bulimia nervosa (BN), and binge-eating disorder (BED) with low birth weight (LBW), preterm birth (PTB), small for gestational age (SGA), large for gestational age (LGA), and miscarriage. Four databases were systematically searched for quantitative literature on maternal EDs that preceded birth outcomes. Eighteen studies met the inclusion criteria and were included in the review. The meta-analyses included 6 studies on miscarriage, 11 on PTB, 4 on LBW, 9 on SGA, and 4 on LGA. The Mantel–Haenszel random effects model was used to test the associations between EDs and birth outcomes. The results showed significant positive associations between AN and LBW (OR 1.74, 95% confidence interval (CI) 1.49, 2.03), AN and SGA (OR 1.39, 95% CI 1.17, 1.65), BN and PTB (OR 1.19, 95% CI 1.04, 1.36), and BED and LGA (OR 1.43 95% CI 1.18, 1.72). EDs were not significantly correlated with miscarriage. These findings reveal the importance of screening for and treating EDs in pregnant women.

Key words: anorexia nervosa, bulimia nervosa, binge-eating disorder, infant, low birth weight, premature birth, small for gestational age, fetal macrosomia, pregnancy.

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RÉSUMÉ

Des revues systématiques antérieures ont fait état de la relation entre les troubles alimentaires (TA) et les issues de grossesse, mais il n'existe aucune méta-analyse sur le sujet. Cette revue systématique et méta-analyse examine l'association entre les TA chroniques maternels, à savoir l'anorexie mentale (AM), la boulimie nerveuse (BN) et l'hyperphagie boulimique (HB), et le faible poids à la naissance (FPN), la naissance prématurée (NP), le petit poids pour l'âge gestationnel (PAG), le gros poids pour l'âge gestationnel (GAG) et les fausses couches. Quatre bases de données ont fait l'objet d'une recherche systématique de la littérature quantitative sur les TA maternels ayant précédé les issues de grossesse. Dix-huit études répondaient aux critères d'inclusion et ont été incluses dans la revue. Les méta-analyses comprenaient 6 études sur les fausses couches, 11 sur la NP, 4 sur le FPN, 9 sur le PAG et 4 sur le GAG. Le modèle à effets aléatoires de Mantel-Haenszel a été utilisé pour tester les associations entre les TA et les issues de grossesse. Les résultats ont montré des associations positives significatives entre l'AM et le FPN (RC 1,74, IC à 95 % : 1,49-2,03), l'AM et le PAG (RC 1,39, IC à 95 % : 1,17-1,65), la BN et la NP (RC 1,19, IC à 95 % : 1,04-1,36), et l'HB et le GAG (RC 1,43, IC à 95 % : 1,18-1,72). Les TA n'étaient pas significativement corrélés avec les fausses couches. Ces résultats révèlent l'importance du dépistage et du traitement des TA chez les femmes enceintes.

Mots-clés : anorexie mentale, boulimie mentale, hyperphagie boulimique, nourrisson, faible poids à la naissance, naissance prématurée, petit pour l'âge gestationnel, fœtal macrosomie, grossesse.

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INTRODUCTION

Women experience many bodily changes throughout pregnancy to prepare for childbirth [1], including increased caloric requirements, increased resting metabolic rate [2], and weight gain [3]. Weight gain can cause immense stress for pregnant women, especially among those with a history of eating disorders (EDs) [4].

EDs are persistent disruptions in eating-related behaviour that lead to abnormal food consumption patterns or malabsorption of nutrients [5]. Anorexia nervosa (AN), bulimia nervosa (BN), and binge-eating disorder (BED) are common EDs among young women in developed countries [6]. AN is characterised by an intense fear of weight gain [7], which can lead to extreme dieting, severe food restriction, and excessive exercise, or binge eating followed by purging [5]. Complications of AN may include amenorrhea, loss of bone mineral density, and vital sign abnormalities [8]. Diagnostic criteria for BN are similar to AN but include binge-eating and compensatory behaviours that occur at least once weekly for a minimum of 3 months [5]. The age of onset for AN [9] and BN [10] is typically during adolescence and young adulthood [11]. The main symptoms of BED include excessive caloric intake in a short period of time, accompanied by the individual's sense of having lost control over their eating behaviour [5].

A study by Easter et al. found that 7.5% of women in the United Kingdom had a diagnosed ED during pregnancy [12]. Another study by Bulik et al. found that the prevalence of EDs during pregnancy was 0.2% for BN and 4.8% for BED [13]. EDs may impact the body's ability to absorb nutrients,

which can have important implications for pregnancy and birth outcomes [5, 14].

Systematic reviews have investigated the association between EDs and birth outcomes. das Neves et al. found that AN and BN are positively associated with low birth weight (LBW), and that BED is associated with higher birth weight and large for gestational age (LGA) [1]. Another systematic review found that AN is associated with miscarriage and preterm birth (PTB), and that BN is associated with giving birth to a small for gestational age (SGA) infant [15]. Reducing the risk of adverse birth outcomes is critical, as they increase the risk for infant morbidity and mortality, as well as the development of chronic health conditions in adulthood [16]. For example, PTB is positively correlated with all-cause mortality in adulthood [17], and both LBW and SGA increase the risk of type 2 diabetes [18].

Currently, no meta-analyses exist that evaluate the relationship between EDs and adverse birth outcomes, thereby allowing for estimation of effect sizes for specific EDs and birth outcomes. This systematic review and meta-analysis examines the association between maternal AN, BN, and BED with the following birth outcomes: LBW, PTB, SGA, LGA, and miscarriage.

METHODS

This review was planned, conducted, and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. The study's protocol was registered on Open Science Framework (https://osf.io/myfbu).

Search strategy

Electronic literature searches were conducted in PubMed, CINAHL, Web of Science, and EMBASE databases. All authors were involved in developing the search strategy, with the help of a health sciences librarian. The search strategy encompassed all relevant literature using keywords (Supplementary Table 1[1]) and subject heading terms adapted to each database. There were no restrictions on language, geographic region, date of publication, or study type. Reference lists of retrieved articles were also examined.

Study eligibility criteria

This review included primary, quantitative studies on women with a history of diagnosed AN, BN, and/or BED. Each study must have also examined the relationship between at least one of these EDs and at least one of the following birth outcomes:

- LBW (<2500 g)
- PTB (<37 weeks gestation)
- SGA (<10th percentile for birth weight)
- LGA (>90th percentile for birth weight)
- Miscarriage (fetal death before 20 weeks of pregnancy).

In addition, an ED diagnosis must have preceded the birth outcome. Qualitative studies, grey literature, articles not written in English, studies in which participants had disordered eating without an ED diagnosis, and studies in which the birth outcome preceded the ED diagnosis were excluded. Two authors (MM and NM) conducted independent title and abstract screening and full-text review with adjudication performed by the principal investigator (JAS) where required.

Study quality assessment

Two authors (MM and NM) independently assessed the methodological quality of nonrandomised studies using the Newcastle–Ottawa scale for cohort studies and case–control studies [19]. Disagreements were resolved by consensus between the authors.

Data extraction

A data extraction sheet was developed using Google Sheets and Microsoft Excel (Microsoft Corporation, Redmond, WA) to retrieve data from each study. The extracted information included author names, year of publication, study design, sample size, geographic location, sociodemographic characteristics, pre-pregnancy body mass index (BMI), gestational weight gain, ED diagnosis, birth outcome(s) assessed, key findings, and study limitations. Two authors (MM and NM) independently coded each study to reduce coding bias.

Evidence synthesis

Two authors (MM and NM) conducted a vote count of all independent statistical tests. Specifically, vote counting was used to assess the relationship between EDs (AN, BN, and BED) and birth outcomes (miscarriage, PTB, LBW, SGA, and LGA) by comparing the number of studies with positive results to the number of studies with negative results. There were insufficient data to conduct a meta-analysis on BED and miscarriage, and BN and LBW. The vote counting focused on the direction of the findings of the main effects, regardless of the statistical significance level. In general, vote counting tends to be very conservative, by accepting the null hypothesis more easily than would be the case using meta-analytic methodology [20]. Once the number of findings in each direction was counted, a sign test was used to assess the cumulative result, such that $Z_{vc} = (N_p) - (½N)/(½\sqrt{N})$, where Z_{vc} is the Z-score for the overall series of findings, N_p is the number of positive findings, and N is the total number of findings (both positive and negative). Since the vote-count method does not provide information on effect size or sample size from each study, average odds ratios (OR) using unweighted and weighted effect sizes were computed using Review Manager (RevMan version 5.4, The Cochrane Collaboration), and a meta-analysis of the association between maternal EDs and

[1]Supplementary data are available with the article at https://dcjournal.ca/doi/suppl/10.3148/cjdpr-2023-019.

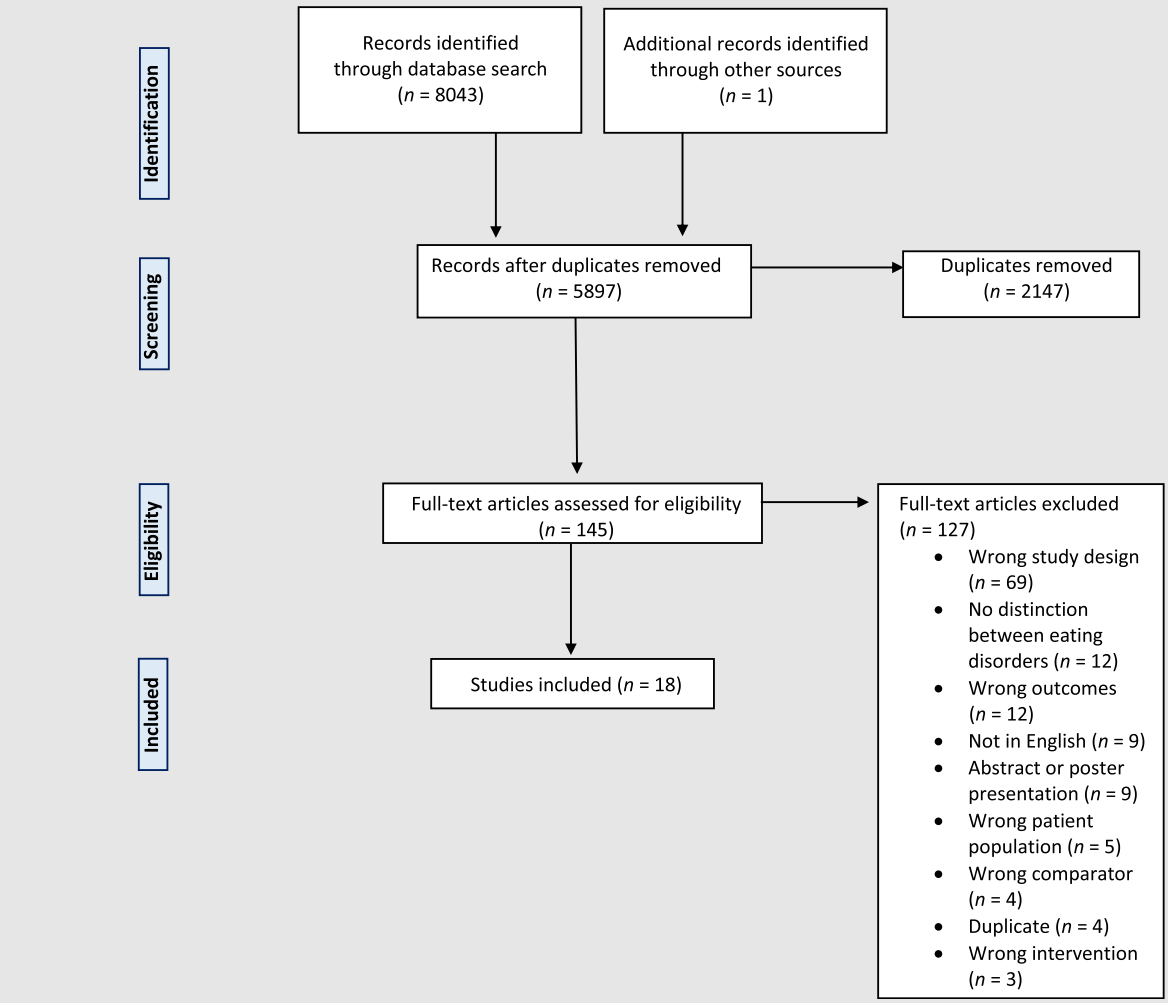
adverse birth outcomes was conducted. Past and current EDs were analyzed as a single group to determine whether lifetime exposure to EDs was associated with adverse birth outcomes, irrespective of the time elapsed between ED recovery and pregnancy for those with past EDs. It was decided a priori that at least three papers were needed for a specific ED and birth outcome (e.g., AN and LBW) to include the pairing in the meta-analysis.

The Mantel–Haenszel random effects model was used to test the association between EDs and birth outcomes, and the OR was the effect measure. The random effects model assumes that both between-study variance and within-study error (i.e., sampling or estimation) are operating and produces larger confidence intervals (CIs), variances, and standard errors than fixed effects models. Random effects models give neither too much weight for studies with a large sample size nor too little weight for studies with a small sample size [21]. Since the purpose of a meta-analysis is to combine studies and pool data to obtain a more precise estimate of effect, the I^2 statistic determined the percentage of variation across studies that is due to heterogeneity and not chance, with I^2 values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively [22]. While clinical heterogeneity always exists in meta-analyses (e.g., differences in patient characteristics, study settings, study design, study quality, exposures, and outcomes), the I^2 provides an assessment of statistical heterogeneity (e.g., inconsistency in findings between studies), where low I^2 values indicate less variability between studies.

RESULTS

The database search resulted in 8,043 records. There were 2,147 duplicates removed and the remaining 5,896 articles were screened by title and abstract. Of those articles, 144 studies met the inclusion criteria for full-text review, and 18 were included (Figure 1). Supplementary Table 2[1] summarises these

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart of the literature search and selection process.



articles. Most studies (95%, n = 17) were cohort studies, and one was case control. The study sample size varied from 51 women [23] to 2,134,495 women [24]. Most studies were conducted in Europe (n = 13), followed by Australia (n = 2), the United States (n = 2), and Canada (n = 1). The publication years ranged from 1991 to 2020. AN was involved in 89% (n = 16) of studies, 72% (n = 13) involved BN, and 33% (n = 6) BED.

Vote count: Maternal EDs and adverse birth outcomes

The results of the vote count show 5 of 5 positive findings between AN and miscarriage (p = 0.03), 7 of 12 for AN and PTB (p = 0.56), 4 of 5 for AN and LBW (p = 0.18), and 9 of 11 for AN and SGA (p = 0.04). With respect to studies on BN, 4 of 4 showed a positive relationship with miscarriage (p = 0.046), 7 of 11 with PTB (p = 0.37), 3 of 4 with LBW (p = 0.32), 7 of 9 with SGA (p = 0.10), and 3 of 5 with LGA (p = 0.66). Findings were positive in the only study on BED and miscarriage, 7 of 11 studies on BED and PTB (p = 0.45), and 4 of 5 studies on BED and LGA (p = 0.18).

Study quality assessment

The results of the quality assessment (Table 1) show that 11 of 18 studies were of good quality, 4 of 18 were of fair quality, and 3 were of poor quality.

Anorexia nervosa

The meta-analyses on AN are shown in Figure 2. The four studies on AN and miscarriage had a combined number of 2,333 participants [25–28]. The pooled OR comparing the prevalence of miscarriage in women with a history of AN was 1.25 (95% CI 0.95, 1.64) with an I^2 statistic of 0%. There were 11 studies on AN and PTB with a combined sample size of 4,318,103 women [24, 25, 28–36]. The pooled OR comparing the prevalence of PTB in AN was 1.18 (95% CI 0.97, 1.44) with an I^2 statistic of 63%. For LBW, the combined number of mothers with AN across the four studies was 2,134,511 [24, 25, 30, 32]. The pooled OR comparing the prevalence of LBW in mothers with AN was 1.74 (95% CI 1.49–2.03) with an I^2 statistic of 0%. The nine studies on AN and SGA had a total of 4,281,430 participants [24, 28–33, 35, 37], a pooled OR of 1.39 (95% CI 1.17–1.65), and an I^2 statistic of 28%.

Bulimia nervosa

The meta-analysis on BN is displayed in Figure 3. Three studies with a total of 2,827 participants were included in the analysis of BN and miscarriage [23, 26, 38]. The pooled OR for this association was 1.60 (95% CI 0.83, 3.11) with an I^2 statistic of 47%. The seven studies on BN and PTB had a combined number of 1,361,209 participants [29, 30, 32–36]. The pooled OR for these studies was 1.19 (95% CI 1.04, 1.36), and the I^2 statistic was 0%. The meta-analysis included six studies on BN and SGA with a total of 1,326,234 participants [29, 30, 32, 33, 35, 37]. The pooled OR was 1.14 (95% CI 0.84–1.54), with an I^2 statistic of 56%. The analysis on BN and LGA was conducted using four studies with a combined number of 1,322,065 participants [26, 29, 33, 37]. The analysis yielded a pooled OR of 1.00 (95% CI 0.85, 1.19) and an I^2 statistic of 0%.

Binge-eating disorder

The meta-analysis on BED and PTB included three studies with a combined sample size of 42,068 women [29, 30, 32]. The pooled OR comparing the prevalence of PTB among women with BED was 1.15 (95% CI 0.93–1.41) and the I^2 statistic was 0%. The meta-analysis on BED and LGA included three studies and 98,480 participants [29, 32, 37]. The analysis yielded an OR of 1.43 (95% CI 1.18–1.72) and an I^2 statistic of 64%. Both results are shown in Figure 4.

DISCUSSION

Main findings

This systematic review and meta-analysis examined the association between maternal EDs and adverse birth outcomes. AN was associated with a 74% increase in the prevalence of LBW and a 39% increase in the prevalence of SGA; BN was associated with a 19% increase in the prevalence of PTB; and BED was associated with a 43% increase in the prevalence of LGA. None of the EDs were significantly associated with miscarriage.

Interpretation

Previous research has found that active BN is associated with higher rates of miscarriage. For example, Morgan et al. found that women with active BN had a 160% increase in odds of miscarriage compared to women with remittent BN (OR 2.6, 95% CI 1.2–5.6) [39]. Similarly, Abraham found that women with active BN had almost twice the frequency of miscarriage than those with remittent ED [38]. This meta-analysis grouped studies on women with lifetime EDs into a single group, which may explain the non-significant results regarding miscarriage. However, research suggests that remission of BN prior to pregnancy may lead to reduction in the risk of miscarriage, but that lifetime exposure to BN may put women at higher risk of miscarriage compared to women who have never suffered from an ED [38, 39]. The analysis of past and current AN as a single group may have also influenced the results of the analysis on PTB. A systematic review by Pan et al found that PTB was among the most commonly reported complications in pregnant women with active AN [40]. The meta-analysis shows a significant positive association between BN and PTB but not AN and PTB. Women with AN or BN are at risk for nutritional deficiencies due to inadequate food intake in AN and purging in some BN patients [30]. Therefore, it is reasonable to expect a higher prevalence of PTB in both AN and BN, but the contradictory meta-analytic findings suggest that the exact mechanism for EDs and PTB is unknown.

Table 1. Quality assessment of the cohort (N = 17) and case control (N = 1) studies investigating the association between maternal eating disorders and adverse birth outcomes using the Newcastle–Ottawa scale.

Cohort studies

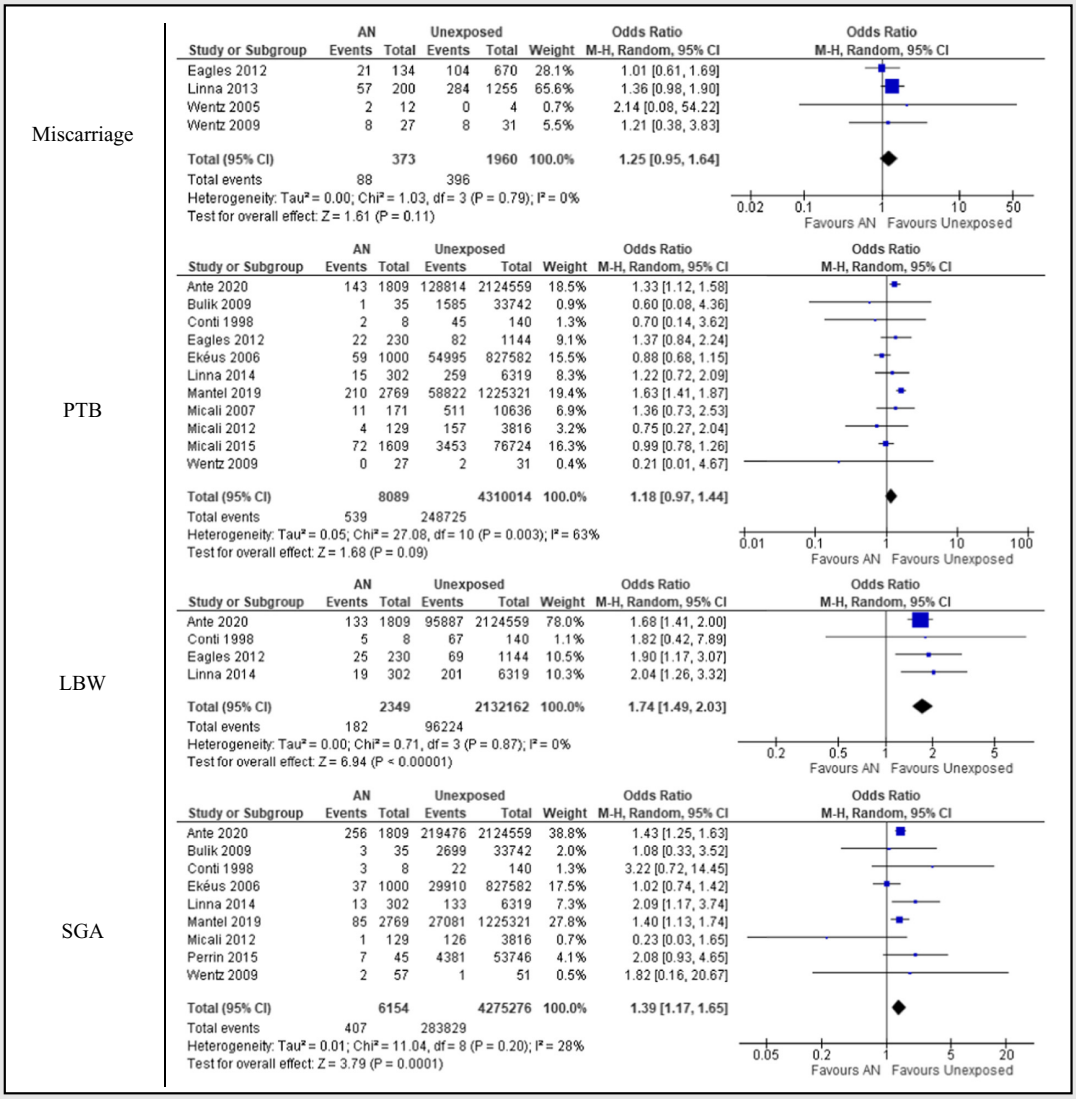
	Selection				Comparability		Outcome			
Authors, Year	**Representativeness of exposed cohort**	**Selection of non-exposed cohort**	**Ascertainment of exposure**	**Demonstration of outcome of interest not present at the start of study**	**Comparable for primary items**	**Comparable for secondary items**	**Assessment of outcomes**	**Follow-up long enough**	**Adequacy of follow-up cohorts**	**Quality**
Abraham (1998) [38]	N	Y	Y	Y	Y	U	Y	Y	Y	Good quality(7/9)
Ante et al. (2020) [24]	N	Y	Y	Y	Y	Y	Y	Y	Y	Good quality (8/9)
Bulik et al. (2009) [29]	N	Y	Y	Y	Y	Y	Y	Y	U	Good quality (7/9)
Eagles et al. (2012) [25]	N	Y	Y	Y	Y	Y	Y	Y	Y	Good quality (8/9)
Ekéus et al. (2006) [31]	N	Y	Y	Y	N	N	Y	Y	Y	Poor quality (6/9)
Linna et al. (2013) [26]	N	Y	Y	Y	Y	N	Y	Y	Y	Good quality (7/9)
Linna et al. (2014) [32]	N	Y	Y	Y	Y	Y	Y	Y	Y	Good quality (8/9)
Mantel et al. (2019) [33]	N	Y	Y	Y	Y	Y	Y	Y	Y	Good quality (8/9)
Micali et al. (2007) [34]	Y	Y	N	U	Y	Y	N	Y	Y	Fair quality (6/9)
Micali et al. (2012) [35]	N	Y	N	Y	Y	Y	Y	Y	N	Fair quality (6/9)
Micali et al. (2015) [36]	N	Y	Y	Y	Y	Y	N	Y	Y	Fair quality (7/9)
Mitchell et al. (1991) [23]	N	Y	Y	Y	Y	N	Y	Y	U	Good quality (6/9)
O'Brien et al. (2017) [48]	N	Y	Y	Y	Y	Y	N	Y	Y	Good quality (7/9)
Perrin et al. (2015) [37]	N	Y	Y	Y	N	Y	N	Y	Y	Good quality (6/9)
Watson et al. (2017) [49]	N	Y	Y	Y	Y	Y	Y	Y	U	Good quality (7/9)
Wentz et al. (2005) [27]	U	Y	Y	Y	Y	Y	N	Y	U	Poor quality (6/9)
Wentz et al. (2009) [28]	U	Y	Y	Y	Y	Y	N	Y	U	Poor quality (6/9)

Case control study

	Selection				Comparability	Exposure			
Authors, year	**Adequate case definition**	**Representativeness of cases**	**Selection of controls**	**Definition of controls**	**Comparability of cases and controls on basis of design or analysis**	**Ascertainment of exposure**	**Same method of ascertainment for cases and control**	**Non-response rate**	**Quality**
Conti et al. (1998) [30]	N	N	Y	Y	Y	Y	Y	N	Fair quality (5/8)

Note: N, no; Y, Yes; U, Unclear. Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain; Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain; Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 star in outcome/exposure domain.

Figure 2. Meta-analyses of the associations between anorexia nervosa (AN) and miscarriage, preterm birth (PTB), low birth weight (LBW), and small for gestational age (SGA). *Note*. Ante et al [24] and Linna et al (2014) [32] 1 birth = 1 woman, for meta-analytic purposes.



The results on AN and LBW are consistent with a 2014 systematic review and meta-analysis showing that AN was associated with a lower birth weight (standardised mean difference −0.19 kg [95% CI −0.25, −0.15]) [41]. The present findings are also in agreement with the systematic review by Pan et al, in which the authors concluded that SGA and LBW were some of the most reported pregnancy complications in women with active AN [40]. Low pre-pregnancy BMI is a risk factor in women with AN for delivering an LBW infant [34]. A Canadian study on risk factors for PTB and SGA found that low pre-pregnancy BMI was associated with SGA [42]. In the study by Eagles et al, more women with AN had a pre-pregnancy BMI under 20 kg/m^2 than women without EDs. They found that women with AN and lower BMIs were more likely to give birth to infants with lower standardised birth weights than women in the same group with a BMI above 20 kg/m^2 [25]. Similarly, in the study by Bulik et al on the Norwegian Mother and Child Cohort (MoBa), mothers with AN had a lower pre-pregnancy BMI, but the rate of SGA was only 0.6% higher than the unexposed control group [29]. This marginal difference might have been due to the fact that MoBa is a population-based cohort, which may represent milder AN cases than hospital-based cohorts [29].

Obesity is common in women with BED, and this, combined with greater gestational weight gain, are potential mediating variables between BED and LGA [32]. Women with a history of BED tend to continue binge eating during

Figure 3. Meta-analyses of bulimia nervosa (BN) and miscarriage, preterm birth (PTB), small for gestational age (SGA), and large for gestational age (LGA). *Note*. Linna et al (2014) [32]: 1 birth = 1 woman, for meta-analytic purposes.

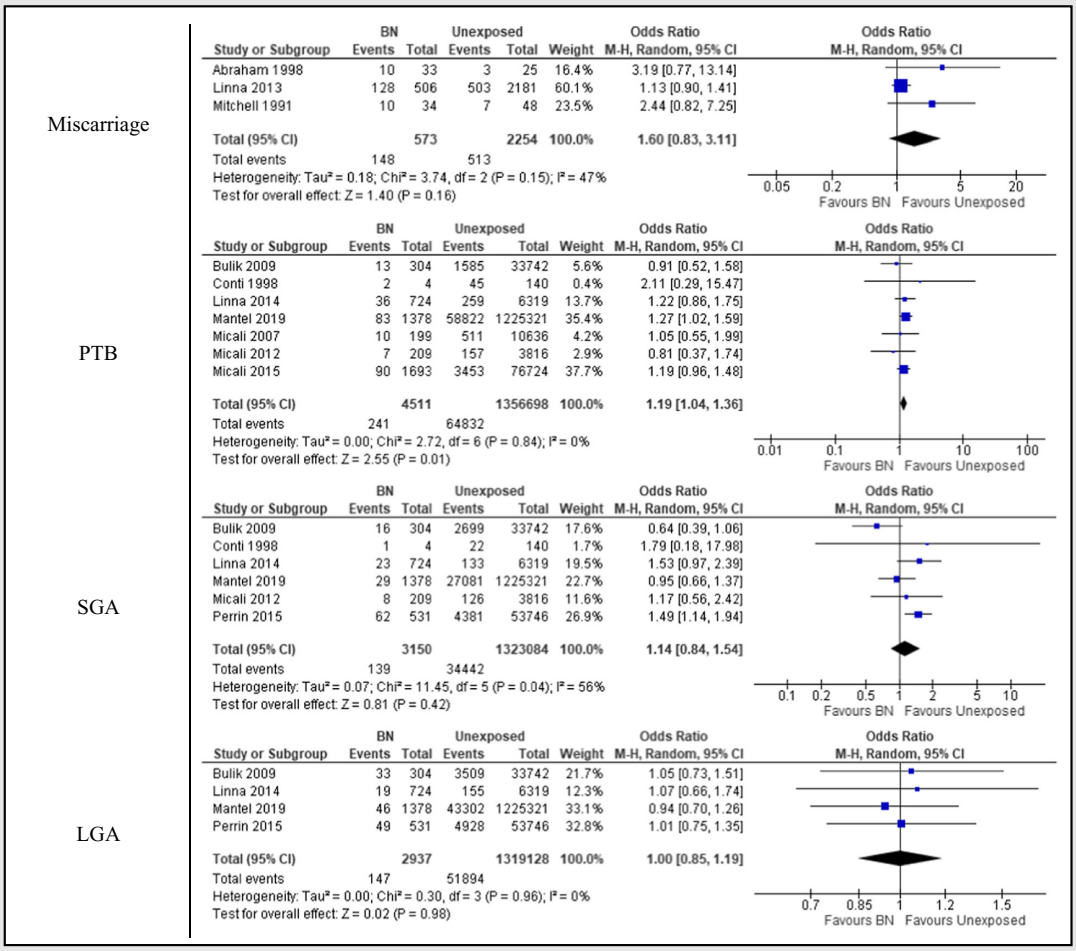
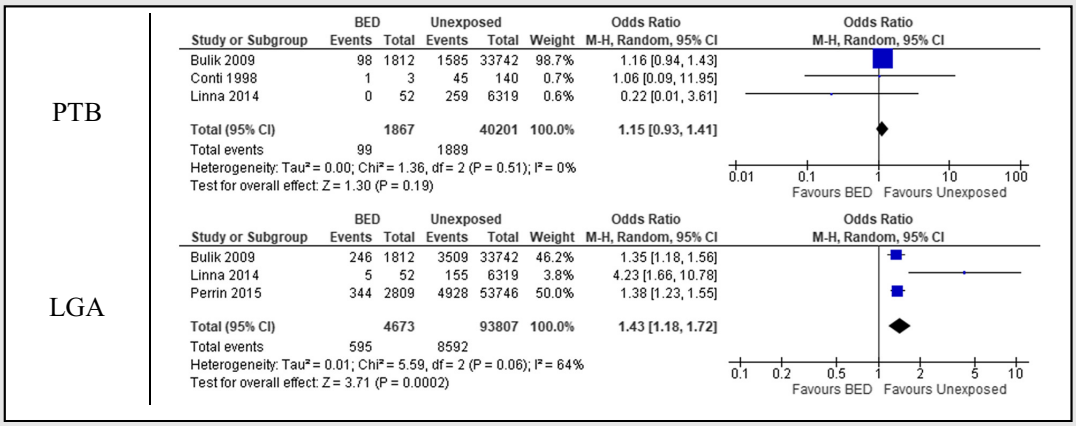


Figure 4. Meta-analyses of the associations between binge-eating disorder (BED) and preterm birth (PTB) and large for gestational age (LGA). *Note*. Linna et al (2014) [32]: 1 birth = 1 woman, for meta-analytic purposes.



pregnancy, and higher gestational weight gain may be the result of high caloric intake over time [29]. Siega-Riz et al found that, on average, women with BED experienced excessive weight gain in pregnancy [4]. A systematic review on maternal
weight gain and fetal growth found that excessive gestational weight gain was associated with LGA [43]. This is opposite to the effects of inadequate gestational weight gain, which is more likely to result in LBW and SGA [43].

Strengths and limitations

This is the first systematic review and meta-analysis to analyze the relationship between diagnosed EDs and birth outcomes. The literature was systematically searched for relevant articles, and the data were pooled to obtain an effect size of the association between each ED and birth outcome. The inclusion of confirmed EDs is a strength of this study as the criteria for diagnosis are firm, objective, and unambiguous. The large sample size for all analyses is another advantage, as it provides greater statistical power to detect clinically meaningful effects, should they exist [44].

The study also comes with limitations. Generalisability may be limited, as all included studies were conducted in developed countries. Many ethnic groups were also underrepresented and the studies did not account for individuals who identify as trans-masculine, non-binary, or other gender-queer identities. Many of the included studies obtained their ED samples from clinical settings, which may be biased towards more severe cases. The inclusion criteria also excluded those diagnosed with other specified feeding or eating disorders, which is an important area of investigation in future research. Gestational weight gain as a potential mediator between EDs and birth outcomes, as well as the relationship between EDs and stillbirth, was intended to be analyzed, but the data were scant and insufficient. Stillbirth is a rare outcome; only 1 in 160 infants is stillborn [45]. Therefore, there is a need for more studies with large sample sizes to capture the prevalence of stillbirth in women with EDs. Future research should also include more diverse populations to increase generalisability of the results.

RELEVANCE TO PRACTICE

EDs create a barrier to consuming an adequate, nutrient-rich diet and may result in nutrient deficiencies [30], underweight [34], or overweight BMI [32]. Weight abnormalities in EDs may mediate their associations with adverse birth outcomes [32, 42]. The findings of this study present a case for providing ED training to healthcare team members such as dietitians, obstetricians and gynecologists, and mental health professionals [46] to better equip them to screen for and treat EDs prior to and during pregnancy [47]. ED remission may reduce the risk of adverse birth outcomes by helping mothers achieve a healthy body weight before pregnancy and promoting adequate weight gain during pregnancy [25, 32, 34, 43].

CONCLUSION

This systematic review and meta-analysis found that AN was positively correlated with LBW and SGA, BN with PTB, and BED with LGA. Factors that may influence birth outcomes within ED populations, such as disease status during pregnancy (active or remittent) and gestational weight gain, should be investigated. Future research on maternal BED and birth outcomes is also needed.

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Conflict of interest: The authors declare that they have no competing interests.

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