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Review

# Maternal and neonatal outcomes in women undergoing bariatric surgery: a systematic review and meta-analysis

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ABSTRACT

*Background:* Obese women are at increased risk for many pregnancy complications, and bariatric surgery (BS) before pregnancy has shown to improve some of these.
*Objectives:* To review the current literature and quantitatively assess the obstetric and neonatal outcomes in pregnant women who have undergone BS.
*Search strategy:* MEDLINE, EMBASE and Cochrane databases were searched using relevant keywords to identify studies that reported on pregnancy outcomes after BS.
*Selection criteria:* Pregnancy outcome in firstly, women after BS compared to obese or BMI-matched women with no BS and secondly, women after BS compared to the same or different women before BS. Only observational studies were included.
*Data collection and analysis:* Two investigators independently collected data on study characteristics and outcome measures of interest. These were analysed using the random effects model. Heterogeneity was assessed and sensitivity analysis was performed to account for publication bias.
*Main results:* The entry criteria were fulfilled by 17 non-randomised cohort or case-control studies, including seven with high methodological quality scores. In the BS group, compared to controls, there was a lower incidence of preeclampsia (OR 0.45, 95% CI 0.25–0.80; $P = 0.007$), GDM (OR 0.47, 95% CI 0.40–0.56; $P < 0.001$) and large neonates (OR 0.46, 95% CI 0.34–0.62; $P < 0.001$) and a higher incidence of small neonates (OR 1.93, 95% CI 1.52–2.44; $P < 0.001$), preterm birth (OR 1.31, 95% CI 1.08–1.58; $P = 0.006$), admission for neonatal intensive care (OR 1.33, 95% CI 1.02–1.72; $P = 0.03$) and maternal anaemia (OR 3.41, 95% CI 1.56–7.44, $P = 0.002$).
*Conclusions:* BS as a whole improves some pregnancy outcomes. Laparoscopic adjustable gastric banding does not appear to increase the rate of small neonates that was seen with other BS procedures. Obese women of childbearing age undergoing BS need to be aware of these outcomes.
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**Contents**



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## Introduction

Obesity in many developed countries is acquiring epidemic proportions. In the UK, one in three pregnant women are overweight or obese [1,2]. In such women, compared to those with normal body mass index (BMI), there is increased risk for many pregnancy complications, including gestational diabetes mellitus (GDM), preeclampsia, preterm birth, anaemia, caesarean section, delivery of small and large neonates and perinatal death [3–11]. Bariatric surgery (BS), including malabsorptive procedures like gastric bypass and restrictive procedures like laparoscopic adjustable gastric band (LAGB), is increasingly being used as an effective method of treating obesity. Several studies including systematic reviews have reported pregnancy outcome following such therapy is improved [12–18]. However, these studies have not been able to quantify the effect by means of meta-analysis because of the insufficient number of suitable primary studies and the heterogeneity among them.

The aim of this study was to review the current literature and quantitatively assess the obstetric and neonatal outcomes in pregnant women who have undergone BS and to examine whether the effects of surgery are the mere consequence of reduction in BMI at the onset of pregnancy.

## Methods

Institutional review board (IRB) approval was not necessary as the meta-analysis did not require any patient identifying information.

### *Selection criteria*

MEDLINE (1966 to June 2014), EMBASE (1980 to June 2014) and Cochrane (1993 to June 2014) databases were searched using the terms "obstetrics AND bariatric surgery", "pregnancy outcomes AND bariatric surgery", "neonatal outcomes AND bariatric surgery" and "Pregnancy outcomes AND weight-reducing surgery".

The inclusion criteria were observational studies reporting on pregnancy outcome in firstly, women after BS compared to obese or BMI-matched women with no BS and secondly, women after BS compared to the same or different women before BS. No language restrictions were made.

The outcome measures of interest were: preeclampsia, GDM, maternal anaemia, preterm birth, caesarean section, large and small neonates, neonatal intensive care admission (NICU) and perinatal mortality.

Two reviewers (NG and ND) independently screened the titles and abstracts from the search to identify all potentially useful studies for which the full manuscripts were evaluated to assess eligibility for the meta-analysis. The reference lists in the selected manuscripts were examined for any additional relevant studies. Any inconsistency regarding the selection of papers was resolved independently by another co-author (CS).

### *Quality assessment*

The quality of the selected studies was evaluated by two assessors (NG and ND) using the Newcastle–Ottawa scale for patient selection, comparability of the two study groups and assessment of outcome [19]. Studies that achieved 9 or more points, from a maximum of 10, were considered to be of high methodological quality.

### *Statistical analysis*

The meta-analysis was performed in line with recommendations from the Cochrane Collaboration and the Quality of Reporting of Meta-analyses guidelines [20,21]. Each outcome measure in the BS group was compared to the control group using the odds ratio (OR) as the summary statistic. Risk ratios were also calculated to determine the percentage increase or decrease of an outcome measure after BS.

In the calculation of ORs the random-effect model was used. This assumes that a variation exists between studies, and therefore the calculated OR has a more conservative value [22,23]. Yate's correction was used for those studies that contained a zero in one cell for the number of events of interest [24,25]. However, such zero values created problems with the computation of ratio and this was overcome by adding 0.5 to each cell of the study in question.

Heterogeneity was evaluated by graphic exploration with funnel plots to assess publication bias and by subgroup analysis using the following: (a) high methodological quality studies comparing pregnancies in women after BS with those in women before or no BS (b) pregnancies in the same women after and before BS, (c) pregnancies in different women after and before BS, (d) pregnancies in women after BS compared to those in women with no BS, but matched to cases for prepregnancy BMI, (e) pregnancies in women after BS compared to those in obese women without BS, but matched to cases for presurgery BMI and (f) pregnancies in women after LAGB with those in women before or no BS.

Analysis was conducted by using the statistical software Review Manager Version 5.2 (The Cochrane Collaboration, Software Update, Oxford, UK).

## Results

*Primary studies included in the meta-analysis*

Search of MEDLINE yielded 312 articles and no additional articles were identified from the searches of the EMBASE and Cochrane databases (Fig. 1). After reading the title and abstract of the studies, 283 were excluded because they were not original cohort studies or did not provide data on the desired pregnancy outcome measures. Full manuscripts were evaluated in 29 cases but only 17 fulfilled the entry criteria [26–42] while the remaining 12 papers were excluded [43–54]. There were three main reasons for excluding these 12 papers: (a) there was no comparison (control) group [44–46,48,50–53], (b) pregnancy outcomes were compared with different timing from BS but not against no surgery [47,54] and (c) different BS techniques were compared against each other but not against no surgery [43,49].

*Main study characteristics and methodological quality assessment*

The 17 articles included in the meta-analysis consisted of 16 retrospective and one prospective [28] non-randomised cohort or case-control studies. High methodological quality scores were obtained for seven of the 17 studies [29,30,33,37,38,41,42]. A total of 166,134 participants were evaluated which included 5361 women after BS and 160,773 controls (Table 1) [26–42]. All studies matched the comparison groups or used logistic regression models to control for confounders.

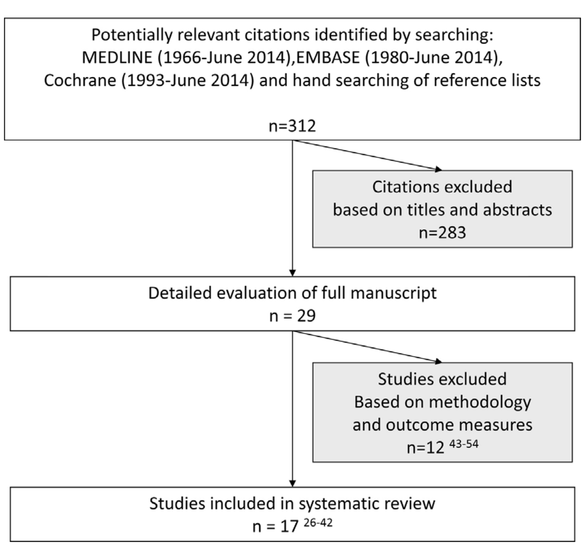


**Fig. 1.** Flowchart showing selection of studies included in the meta-analysis.

*Definitions of outcome measures*

*Preeclampsia*

This was reported in 11 of the 17 studies [27–31,33,36–38,40,42], but only two provided a definition for the condition [33,38]. In both studies, preeclampsia was defined as systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg after 20 weeks' gestation in previously normotensive women together with proteinuria (>100 mg/dL on urinalysis or 300 mg in a 24-h urine collection).

*Gestational diabetes*

This was reported in 15 of the 17 studies [26–34,36–40,42], but only two provided a definition for the condition [32,33]. One study defined GDM as the new incidence of abnormal glucose tolerance complicating pregnancy, childbirth or puerperium [32] and the other [33] defined GDM as per the Carpenter–Courstan criteria and the recommendations after a 100 g oral glucose tolerance test [55,56].

*Maternal anaemia*

This was reported in four of the 17 studies and all defined it as haemoglobin concentration less than 10 g/dL [30,34,36,42]. None of the studies specified the gestational age at which blood samples were taken.

*Caesarean section*

This was reported in 13 of the 17 [26,27,29,30,32–40] studies and in all but one [27] data were provided for total rather than emergency or elective caesarean section.

*Preterm birth*

This was reported in 12 of the 17 studies [26,28,29,33–41]. In eight studies, preterm birth was defined as birth before the 37th week of gestation, but in four studies no definition was provided [26,34,36,38]. Only one study provided separate data on spontaneous and iatrogenic preterm birth [41].

*Large neonates*

This was reported in 14 of the 17 studies [26,28–30,32,33,35–42] and in 11 of these it was defined as macrosomia in which the birth weight was over 4 kg [26,28–30,33,36–40,42]. Two studies reported incidence of large for gestational age, defined as birth weight above the 95th percentile [35,41], another provided data separately for macrosomia and large for gestational age above the 90th percentile [33] and another reported macrosomia and LGA together but no definition was provided for either [32]. For the purpose of this study all the above outcomes were classified as large neonates.

*Small neonates*

This was reported in 11 of the 17 studies [28–30,33–38,40,41] and in three of these it was defined as intrauterine growth restriction (IUGR) [30,34,36]. However, only one provided a definition of IUGR as a decrease in fetal growth velocity in serial ultrasound scans [34]. Seven studies reported on small for gestational age neonates, which was defined as birth weight below the 10th percentile [29,33,37,38] or below the 5th percentile [35,40,41]. Low birth weight (LBW) was reported in three studies; this was defined as weight less than 2.5 kg in two [28,29], whereas one study did not provide a definition for LBW [30]. In these three studies, LBW was not associated with prematurity and was thought to be the result of the micronutrient restriction seen after bariatric surgery [28–30]. Since different terms were used which were not even consistently defined, the authors decided to collectively group the above outcomes to the "small neonates"

**Table 1**
The main characteristics of each study with the methodological quality score.

| Study | Study design | Case group | Control group | Newcastle–Ottawa |
|---|---|---|---|---|
| Wittgrove et al. [26] | Case-control, retrospective | 18 | 23 Same women before BS | 8/10 |
| Skull et al. [27] | Case-control, retrospective | 49 | 31 Same women before BS | 8/10 |
| Dixon et al. [28] | Case-control, prospective | 79 | A: 40 Same women before BS<br>B: 79 Different obese women with no BS, matched for pre surgery BMI | 8/10 |
| Ducarme et al. [29] | Case-control, retrospective | 13 | 414 Different obese women with no BS | 9/10 |
| Weintraub et al. [30] | Cohort, retrospective | 507 | 301 Different obese women before BS | 9/10 |
| Bennett et al. [31] | Cohort, retrospective | 316 | 269 Different obese women before BS | 7/10 |
| Burke et al. [32] | Case-control, retrospective | 354 | 346 Different obese women before BS | 7/10 |
| Lapolla et al. [33] | Cohort, retrospective<br>Case-control, retrospective | A: 83<br>B: 27 | A: 120 Different obese women with no BS<br>B: 27 Different obese women before BS | 10/10 |
| Santulli et al. [34] | Cohort, retrospective | 24 | 120 Different obese women with no BS, matched for prepregnancy BMI | 8/10 |
| Josefsson et al. [35] | Cohort, retrospective | 126 | 241 Different obese women before BS | 8/10 |
| Aricha-Tamir et al. [36] | Case-control, retrospective | 144 | 144 Same women before BS | 8/10 |
| Belogolovkin et al. [37] | Cohort, retrospective | 293 | 131,023 Different obese women with no BS | 10/10 |
| Lesko et al. [38] | Case-control, retrospective | 70 | A: 140 Different obese women with no BS, matched for presurgery BMI<br>B: 140 Different obese women with no BS, matched for prepregnancy BMI | 10/10 |
| Amsalem et al. [39] | Case-control, retrospective | 109 | 109 Same women before BS | 8/10 |
| Kjaer et al. [40] | Case-control, retrospective | 339 | 1277 Different obese women with no BS, matched for prepregnancy BMI | 8/10 |
| Roos et al. [41] | Case-control, retrospective | A: 2474<br>B: 2511 | A: 11,979 Different obese women with no BS, matched for presurgery BMI<br>B: 12,379 Different obese women with no BS, matched for prepregnancy BMI | 9/10 |
| Shai et al. [42] | Case-control, retrospective | 326 | 1612 Different obese women with no BS | 9/10 |

A = deliveries in women after bariatric surgery (BS); B = deliveries in women before or no bariatric surgery (BS).

**Table 2**
Results of overall meta-analysis.

| Outcome of interest | Studies | Participants | | OR (95% CI) | *P*-value | Heterogeneity *P*-value | RR (95% CI) |
|---|---|---|---|---|---|---|---|
| | | BS | Control | | | | |
| Preeclampsia | 11 | 2075 | 135,473 | 0.45 (0.25–0.80) | 0.007 | <0.001 | 0.48 (0.29–0.82) |
| Gestational diabetes mellitus | 15 | 2724 | 136,075 | 0.47 (0.40–0.56) | <0.001 | <0.001 | 0.52 (0.45–0.59) |
| Preterm birth | 12 | 3809 | 158,263 | 1.31 (1.08–1.58) | 0.006 | 0.022 | 1.28 (1.08–1.51) |
| Large neonates | 14 | 4968 | 148,334 | 0.46 (0.34–0.62) | <0.001 | 0.004 | 0.51 (0.38–0.67) |
| Small neonates | 11 | 4185 | 158,343 | 1.93 (1.52–2.44) | <0.001 | 0.012 | 1.83 (1.48–2.27) |
| Maternal anaemia | 4 | 1270 | 133,170 | 3.41 (1.56–7.44) | 0.002 | <0.001 | 2.63 (1.25–5.53) |
| Caesarean section | 13 | 2126 | 134,456 | 0.99 (0.75–1.31) | 0.95 | <0.001 | 1.00 (0.84–1.20) |
| Perinatal mortality | 5 | 3804 | 14,532 | 1.05 (0.48–2.31) | 0.90 | 0.15 | 1.05 (0.48–2.28) |
| Neonatal intensive care | 4 | 516 | 1824 | 1.38 (1.02–1.86) | 0.03 | 0.51 | 1.33 (1.02–1.72) |

BS = bariatric surgery, OR = odds ratio, RR = risk ratio, CI = confidence interval.

as the ultimate end point, albeit this could be the result of different mechanism.

*Perinatal mortality*

This was reported in five of the 17 studies [30,32,38,40,41]. One did not give a definition [38], three presented data only on fetal death between 22 and 40 weeks' gestation [30,32,41] while Kjaer et al. defined perinatal mortality as death from 22 weeks' gestation to the 7th day postpartum [40].

*Neonatal intensive care admissions*

This was reported in four of the 17 studies [33,34,38,40]. None of the studies provided information on the indication of admission or the length of stay.

*Results for the overall meta-analysis*

Table 2 and Fig. 2 summarise the obstetric and neonatal outcomes in women who underwent BS and the controls. In the BS group, compared to controls, there was a lower incidence of preeclampsia (OR 0.45, 95% CI 0.25–0.80; $P = 0.007$), GDM (OR 0.47, 95% CI 0.40–0.56; $P < 0.001$) and large neonates (OR 0.46, 95% CI 0.34–0.62; $P < 0.001$) and a higher incidence of small neonates (OR 1.93, 95% CI 1.52–2.44; $P < 0.001$), preterm birth (OR 1.31, 95% CI 1.08–1.58; $P = 0.006$), admission for neonatal intensive care (OR 1.33, 95% CI 1.02–1.72; $P = 0.03$) and maternal anaemia (OR 3.41, 95% CI 1.56–7.44, $P = 0.002$). There were no significant differences

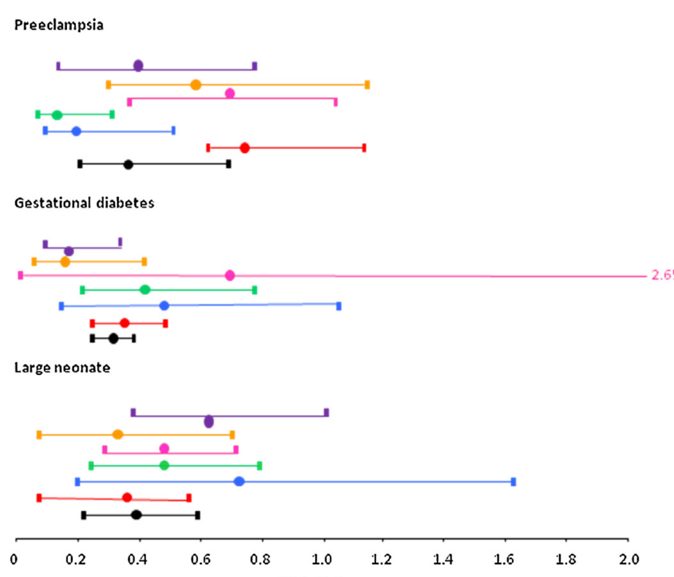


**Fig. 2.** Summary of odds ratio with 95% confidence interval for preeclampsia, gestational diabetes mellitus and birth of large neonates in pregnancies of women who underwent bariatric surgery (BS) compared to those in controls. Total analysis (black), high methodological quality studies (red), after and before BS in the same women (blue), after and before BS in different women (green), after BS compared to women with no BS, but matched to cases for prepregnancy BMI (pink) and after BS compared to women without BS, but matched to cases for presurgery BMI (brown).

**Table 3**
Results of meta-analysis in the subgroup of high methodological quality studies comparing outcome in pregnancies of women after bariatric surgery to those of obese women before or no surgery.

| Outcome of interest | References of studies | Participants | | OR (95% CI) | P-value | Heterogeneity P-value | RR (95% CI) |
|---|---|---|---|---|---|---|---|
| | | BS | Control | | | | |
| Preeclampsia | [29,30,33,37,38,42] | 1292 | 133,777 | 0.76 (0.52–1.11) | 0.16 | 0.16 | 0.78 (0.55–1.11) |
| Gestational diabetes mellitus | [29,30,33,37,38,42] | 1292 | 133,777 | 0.34 (0.18–0.67) | <0.001 | <0.001 | 0.41 (0.23–0.72) |
| Preterm birth | [33,37,38,41] | 2,957 | 155,856 | 1.51 (1.33–1.72) | <0.001 | 0.59 | 1.46 (1.30–1.63) |
| Large neonates | [29,30,33,37,38,41,42] | 3799 | 146,115 | 0.38 (0.24–0.58) | <0.001 | 0.009 | 0.42 (0.28–0.63) |
| Small neonates | [29,30,33,37,38,41] | 3473 | 156,482 | 1.88 (1.42–2.50) | <0.001 | 0.09 | 1.80 (1.41–2.30) |
| Maternal anaemia | [37,42] | 619 | 132,635 | 2.40 (0.97–5.96) | 0.06 | <0.001 | 2.00 (0.82–4.89) |
| Caesarean section | [29,30,33,37,38] | 966 | 132,165 | 1.01 (0.63–1.63) | 0.96 | <0.001 | 1.04 (0.77–1.40) |
| Perinatal mortality | [30,38] | 577 | 581 | 2.35 (0.06–89.67) | 0.65 | 0.003 | 2.31 (0.06–82.26) |
| Neonatal intensive care | [33,38] | 153 | 427 | 1.56 (0.73–3.36) | 0.25 | 0.17 | 1.48 (0.77–2.83) |

BS = bariatric surgery, OR = odds ratio, RR = risk ratio, CI = confidence interval.

**Table 4**
Results of meta-analysis in the subgroup of studies comparing outcome in pregnancies of women after bariatric surgery and those in the same women before surgery.

| Outcome of interest | References of studies | Participants | | OR (95% CI) | P-value | Heterogeneity P-value | RR (95% CI) |
|---|---|---|---|---|---|---|---|
| | | BS | Control | | | | |
| Preeclampsia | [27,28,33] | 155 | 98 | 0.20 (0.08–0.51) | <0.001 | 0.56 | 0.24 (0.11–0.56) |
| Gestational diabetes mellitus | [26,28,33,36,39] | 377 | 343 | 0.71 (0.45–0.1.11) | 0.14 | <0.001 | 0.73 (0.48–1.10) |
| Preterm birth | [26,33,36,39] | 298 | 303 | 0.75 (0.45–1.26) | 0.28 | 84 | 0.78 (0.49–1.23) |
| Large neonates | [26,33,36,39] | 298 | 303 | 0.75 (0.35–1.63) | 0.47 | 0.19 | 0.81 (0.44–1.50) |
| Small neonates | [33,36] | 171 | 171 | 0.81 (0.16–4.00) | 0.79 | 0.26 | 0.83 (0.18–3.77) |
| Maternal anaemia | – | | | | | | |
| Caesarean section | [26,27,33,36,39] | 344 | 334 | 1.26 (0.87–1.83) | 0.22 | 0.35 | 1.18 (0.92–1.52) |
| Perinatal mortality | – | | | | | | |
| Neonatal intensive care | – | | | | | | |

BS = bariatric surgery, OR = odds ratio, RR = risk ratio, CI = confidence interval.

between the groups in incidence of caesarean section or perinatal mortality.

### *Subgroup analysis*

The findings of subgroup analysis for the following: (a) high methodological quality studies comparing pregnancies in women after BS with those in women before or no BS, (b) pregnancies in the same women after and before BS, (c) pregnancies in different women after and before BS, (d) pregnancies in women after BS compared to those in women with no BS, but matched to cases for prepregnancy BMI, (e) pregnancies in women after BS compared to those in obese women without BS, but matched to cases for presurgery BMI and (f) pregnancies in women after LAGB with those in women before or no BS are summarised in Tables 3–8. The results of the total and subgroup analysis for preeclampsia, GDM, large and small neonates and caesarean section are illustrated in Figs. 2 and 3.

### *Publication bias*

Evaluation of funnel plots demonstrated publication bias was present for preeclampsia and large neonates, even after sensitivity analysis of high methodological quality studies. A funnel plot of all the studies used in the meta-analysis reporting on GDM is shown in Fig. 4 (top). All studies (except from two [28,30]) lie inside the 95% CIs and are distributed evenly about the vertical, showing no evidence of publication bias. Heterogeneity was observed among the studies ($P = 0.001$). When only high methodological quality studies were considered (Fig. 4, bottom) all studies lied within the 95% CIs and were distributed evenly about the vertical, showing no evidence of publication bias ($P = 0.55$).

**Table 5**
Results of meta-analysis in the subgroup of studies comparing outcome in pregnancies of women after bariatric surgery and those in a different group of women before surgery.

| Outcome of interest | References of studies | Participants | | OR (95% CI) | P-value | Heterogeneity P-value | RR (95% CI) |
|---|---|---|---|---|---|---|---|
| | | BS | Control | | | | |
| | | BS | Control | | | | |
| Preeclampsia | [30,31] | 823 | 570 | 0.14 (0.06–0.31) | <0.001 | 0.18 | 0.16 (0.10–0.27) |
| Gestational diabetes mellitus | [30–32] | 1171 | 916 | 0.42 (0.22–0.79) | 0.007 | 0.002 | 0.48 (0.29–0.81) |
| Preterm birth | – | | | | | | |
| Large neonates | [30,32] | 987 | 888 | 0.52 (0.31–0.86) | 0.01 | 0.16 | 0.54 (0.32–0.92) |
| Small neonates | [30,35] | 633 | 542 | 1.58 (1.02–2.45) | 0.04 | 0.31 | 1.54 (0.95–2.50) |
| Maternal anaemia | – | | | | | | |
| Caesarean section | [30,32,35] | 987 | 888 | 0.92 (0.38–2.22) | 0.82 | <0.001 | 0.96 (0.51–1.81) |
| Perinatal mortality | [30,32] | 861 | 647 | 0.52 (0.19–1.41) | 0.20 | 0.47 | 0.52 (0.20–1.40) |
| Neonatal intensive care | – | | | | | | |

BS = bariatric surgery, OR = odds ratio, RR = risk ratio, CI = confidence interval.

**Table 6**
Results of meta-analysis in the subgroup of studies comparing outcome in pregnancies of women after bariatric surgery and those in obese women without surgery, but matched for prepregnancy body mass index.

| Outcome of interest | References of studies | Participants | | OR (95% CI) | *P*-value | Heterogeneity *P*-value | RR (95% CI) |
|---|---|---|---|---|---|---|---|
| | | BS | Control | | | | |
| Preeclampsia | [38,40] | 407 | 1417 | 0.63 (0.38–1.06) | 0.08 | 0.53 | 0.67 (0.42–1.07) |
| Gestational diabetes mellitus | [34,38,40] | 433 | 1537 | 0.77 (0.22–2.65) | 0.68 | 0.10 | 0.81 (0.26–2.51) |
| Preterm birth | [34,38,40,41] | 2944 | 13,916 | 1.67 (1.27–2.18) | <0.001 | 0.26 | 1.60 (1.27–2.02) |
| Large neonates | [40,41] | 2916 | 13,755 | 0.44 (0.27–0.70) | <0.001 | 0.17 | 0.46 (0.30–0.72) |
| Small neonates | [34,38,40,41] | 2940 | 13,875 | 2.30 (1.53–3.44) | <0.001 | 0.16 | 2.18 (1.51–3.13) |
| Maternal anaemia | – | | | | | | |
| Caesarean section | [34,38,40] | 433 | 1537 | 1.16 (0.92–1.46) | 0.20 | 0.78 | 1.11 (0.95–1.30) |
| Perinatal mortality | [38,40] | 409 | 1417 | 2.08 (0.14–30.87) | 0.60 | 0.08 | 2.04 (0.14–28.75) |
| Neonatal intensive care | [34,38,40] | 433 | 1537 | 2.00 (0.80–4.99) | 0.14 | 0.08 | 1.87 (0.81–4.34) |

BS = bariatric surgery, OR = odds ratio, RR = risk ratio, CI = confidence interval.

**Table 7**
Results of meta-analysis in the subgroup of studies comparing outcome in pregnancies of women after bariatric surgery and those in obese women without surgery, but matched for presurgery body mass index.

| Outcome of interest | References of studies | Participants | | OR (95% CI) | *P*-value | Heterogeneity *P*-value | RR (95% CI) |
|---|---|---|---|---|---|---|---|
| | | BS | Control | | | | |
| Preeclampsia | [28,29,33,37,38,42] | 864 | 133,388 | 0.69 (0.43–1.12) | 0.13 | 0.05 | 0.73 (0.48–1.11) |
| Gestational diabetes mellitus | [28,29,33,37,38,42] | 864 | 133,388 | 0.24 (0.10–0.54) | <0.001 | <0.001 | 0.30 (0.15–0.61) |
| Preterm birth | [28,33,37,38,41] | 2999 | 142,489 | 1.35 (1.18–1.54) | <0.001 | 0.43 | 1.32 (1.17–1.48) |
| Large neonates | [28,29,33,37,38,42] | 864 | 133,388 | 0.35 (0.18–0.66) | 0.001 | 0.02 | 0.39 (0.20–0.76) |
| Small neonates | [28,29,33,37,38,41] | 3008 | 143,755 | 1.90 (1.39–2.77) | <0.001 | 0.14 | 1.84 (1.41–2.40) |
| Maternal anaemia | [37,42] | 619 | 132,635 | 2.40 (0.97–5.96) | 0.06 | <0.001 | 2.00 (0.82–4.89) |
| Caesarean section | [29,33,37,38] | 459 | 131,697 | 0.69 (0.34–1.42) | 0.32 | <0.001 | 0.84 (0.57–1.23) |
| Perinatal mortality | – | | | | | | |
| Neonatal intensive care | [33,38] | 153 | 260 | 2.27 (1.26–4.07) | 0.006 | 0.93 | 2.03 (1.22–3.36) |

BS = bariatric surgery, OR = odds ratio, RR = risk ratio, CI = confidence interval.

**Table 8**
Results of meta-analysis in the subgroup of studies comparing outcome in pregnancies of women after LAGB and those in obese women with no BS.

| Outcome of interest | References of studies | Participants | | OR (95% CI) | *P*-value | Heterogeneity *P*-value | RR (95% CI) |
|---|---|---|---|---|---|---|---|
| | | BS | Control | | | | |
| Preeclampsia | [27–29,33] | 224 | 711 | 0.34 (0.14–0.81) | 0.01 | 0.20 | 0.39 (0.18–0.85) |
| Gestational diabetes mellitus | [27–29, 33] | 224 | 711 | 0.16 (0.09–0.32) | <0.001 | 0.35 | 0.22 (0.13–0.38) |
| Preterm birth | [28,29,33] | 175 | 640 | 0.99 (0.43–2.30) | 0.98 | 0.21 | 0.99 (0.47–2.09) |
| Large neonates | [28,29,33] | 175 | 640 | 0.62 (0.38–1.00) | 0.05 | 0.97 | 0.71 (0.49–1.01) |
| Small neonates | [28,29,33] | 175 | 640 | 0.57 (0.22–1.44) | 0.23 | 0.68 | 0.60 (0.25–1.42) |
| Maternal anaemia | – | | | | | | |
| Caesarean section | [27,29,33] | 145 | 592 | 0.74 (0.29–1.90) | 0.54 | 0.08 | 0.87 (0.47–1.58) |
| Perinatal mortality | – | | | | | | |
| Neonatal intensive care | – | | | | | | |

LAGB = laparoscopic adjustable gastric band, BS = bariatric surgery, OR = odds ratio, RR = risk ratio, CI = confidence interval.

## Discussion

### *Main findings*

The findings of this meta-analysis demonstrate that in women who underwent BS, compared to controls without BS, there is a decrease in the incidence of preeclampsia, GDM and large neonates, an increase in the incidence of small neonates, preterm birth, admission for neonatal intensive care, maternal anaemia and no significant difference in incidence of caesarean section or perinatal mortality.

Interpretation

### *Preeclampsia*

There is a well-reported association between obesity and the development of preeclampsia [57,58]. There is also good evidence that the incidence of preeclampsia is decreased by BS [13,14,16,18]. This meta-analysis has confirmed that BS is associated with reduction in preeclampsia and has quantified this effect as being about half.

### *Gestational diabetes mellitus*

Previous systematic reviews have concluded that the incidence of GDM is reduced in women who had BS before pregnancy compared to obese women [13,14,16,18]. Our meta-analysis quantifies this effect as being about half.

It has been previously speculated that this reduction in the incidence of GDM might be due to the metabolic or absorptive changes that occur in response to BS [38]. In addition, studies investigating post-BS pregnancies with those of the general population, found that the incidence of GDM was higher in the post-BS group [12,59]. Our subgroup analysis revealed no significant difference in GDM between post-BS pregnancies and pregnancies with matched prepregnancy BMI ($P = 0.68$). This

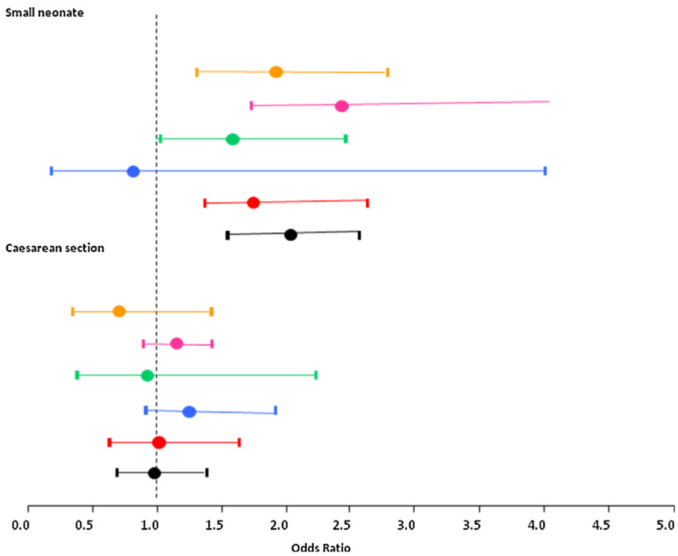


**Fig. 3.** Summary of odds ratio with 95% confidence interval for birth of small neonates and caesarean section in pregnancies of women who underwent bariatric surgery (BS) compared to those in controls. Total analysis (black), high methodological quality studies (red), after and before BS in the same women (blue), after and before BS in different women (green), after BS compared to women with no BS, but matched to cases for prepregnancy BMI (pink) and after BS compared to women without BS, but matched to cases for presurgery BMI (brown).

suggests that BMI and the hormonal and metabolic environment associated with it are responsible for the development or worsening of diabetes and not the postoperative status per se.

## Small and large neonates

Previous systematic reviews have concluded that in women who had BS before pregnancy, compared to obese pregnant women, the incidence of large neonates is reduced and that of small neonates is increased [13,14,16–18]. The present meta-analysis found that the risk of large neonates is halved and that of small neonates is increased by about 80%.

Our subgroup analysis revealed that unlike the case of GDM, the incidence of small neonates in the BS group was significantly

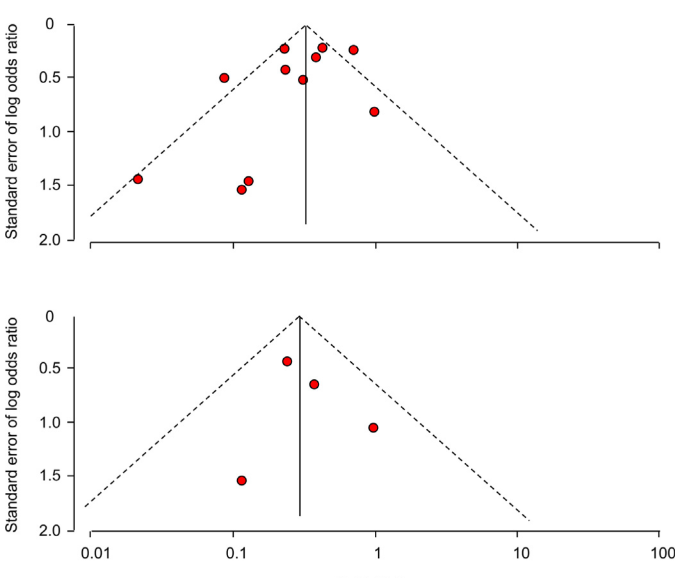


**Fig. 4.** Funnel plot illustrating heterogeneity in regards to the incidence of gestational diabetes mellitus in the overall meta-analysis (top) and in the sensitivity analysis of high methodological quality studies (bottom).

higher than in pregnancies with matched prepregnancy BMI. It was previously suggested that the BS-related increase in incidence of small neonates is the consequence of malnutrition and microenvironment deficiencies secondary to the therapeutic postoperative state [18]. Interestingly, a subgroup analysis of women who had undergone LAGB compared to women with no surgery, found no difference in the rates of small neonates ($P = 0.23$). This suggests that restrictive rather than malabsorptive BS (like gastric bypass) should be preferred in young women planning to have children in order to minimise this complication.

This issue requires further investigation because the beneficial long-term effects in the reduction of large neonates in regards to obesity and type 2 diabetes [15] may be counterbalanced by the detrimental effects of fetal growth restriction [60,61].

## Preterm birth

This meta-analysis found that BS is associated with a 28% increase in preterm birth. Similarly, subgroup analysis on prepregnancy BMI-matched obese women and on high methodological quality studies also found that in the BS group there is an increase in the incidence of preterm birth. These findings contradict those of a previous review which reported that BS is associated with a decrease in preterm birth [13]. The studies did not report on spontaneous or iatrogenic preterm birth separately.

In the subgroup analysis of women who had undergone LAGB compared to women with no surgery, there was no difference in the rate of preterm birth ($P = 0.98$). Therefore, our findings may be related to the increase in small neonates after BS as a whole, but not after LAGB, which is likely to cause iatrogenic rather than spontaneous preterm birth. This, however, requires further investigation.

## Caesarean section

There was considerable inconsistency in the literature regarding the incidence of caesarean section after BS. One systematic review concluded that the incidence of caesarean section after BS is increased compared to that of obese women with no BS [14]. Moreover, one primary study investigating pregnancy outcomes after BS compared to the normal population concluded that BS is an independent risk factor for caesarean section [59]. The authors of the same study acknowledged the absence of any possible physiological cause for such effect and concluded that this may be a result of care-giver bias. On the other hand, a review by Vrebosch et al. found that the incidence of caesarean sections was lower after BS [16]. Two other reviews concluded that the incidence of caesarean section after BS is unclear and will need to be investigated further [13,18].

Our meta-analysis did not demonstrate any significant difference in caesarean section rates in women after BS, compared to obese women with no BS, in either the total group analysis or any of the subanalyses. We conclude that BS does not appear to have an effect on the rate of caesarean section.

## Maternal anaemia

The present study found significant increase in the incidence of anaemia in pregnant women after BS, compared to obese women with no BS. However, only four studies contributed to this meta-analysis [30,36,37,42]. Obesity is associated with poor iron status and higher iron requirements [62]. Moreover, Salgado et al. reported an increased iron loss and decreased iron absorption after BS [63]. The same study also found that the incidence of anaemia post BS was higher in younger and in female patients.

We suggest that these women should have more frequent haematological investigations during pregnancy in order to receive prompt and effective supplementation. This may avoid the need of blood transfusion after delivery which was reported to be higher after BS in one study [38].

*Strengths and limitations*

This is the first meta-analysis exploring the obstetric and neonatal outcomes after BS. A total number of 166,134 participants were taken into account and six different subgroups were created to provide more information and minimise potential bias.

Meta-analyses are thought to provide the highest level of evidence [64], but they have been criticised in that they reinforce the inherent systematic biases of the included studies, produce spurious statistical stability and discourage further research [65]. On the other hand, it is argued that pooling results from many primary studies and statistical quantification provide an excellent tool for identifying reasons for variability and inconsistency and that the finding of heterogeneity sets the stage for further research on a given topic [66].

Given that randomised control trials are not feasible for assessing pregnancy outcomes, observational studies represent the best available evidence. However, such studies are subject to confounding and bias [67]. The results of this meta-analysis should be interpreted with caution because of the retrospective nature of the included studies, the varied definitions of the outcome measures and heterogeneity between the individual studies that occasionally persisted during subgroup analysis. Furthermore, most studies did not provide separate data on each BS procedure, but rather presented pregnancy outcome after BS as a whole. Four studies compared pregnancy outcome in women who underwent LABG only and these were presented as a subgroup [27–29,33]. Future studies will need to compare pregnancy outcome between different BS procedures. Finally, the studies included did not provide separate data on the outcomes in regard to the time from BS in order to identify the optimum time for conception after BS. However, this question has been specifically addressed elsewhere [54].

## Conclusion

The present study concludes that BS improves pregnancy outcomes but potentially increases the risk of small neonates and preterm birth. However, these complications disappear after LAGB which should be the preferred procedure in women planning to become pregnant. This meta-analysis should be regarded as a valuable working document for the growing number of healthcare professionals who need to be aware of the pregnancy outcomes after BS in order to inform when caring for obese women of childbearing age.

## Contribution to authorship

N Galazis: Performed the literature search, data analysis and composed first draft.

N Docheva: Performed literature search and extraction of relevant study characteristics.

C Simillis: Performed the statistical analysis.

KH Nicolaides: Supervised work throughout and composed second, third and fourth drafts.

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