ORIGINAL ARTICLE

Outcomes of Pregnancy after Bariatric Surgery

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ABSTRACT

BACKGROUND
Maternal obesity is associated with increased risks of gestational diabetes, large-for-gestational-age infants, preterm birth, congenital malformations, and stillbirth. The risks of these outcomes among women who have undergone bariatric surgery are unclear.

METHODS
We identified 627,693 singleton pregnancies in the Swedish Medical Birth Register from 2006 through 2011, of which 670 occurred in women who had previously undergone bariatric surgery and for whom presurgery weight was documented. For each pregnancy after bariatric surgery, up to five control pregnancies were matched for the mother's presurgery body-mass index (BMI; we used early-pregnancy BMI in the controls), age, parity, smoking history, educational level, and delivery year. We assessed the risks of gestational diabetes, large-for-gestational-age and small-for-gestational-age infants, preterm birth, stillbirth, neonatal death, and major congenital malformations.

RESULTS
Pregnancies after bariatric surgery, as compared with matched control pregnancies, were associated with lower risks of gestational diabetes (1.9% vs. 6.8%; odds ratio, 0.25; 95% confidence interval [CI], 0.13 to 0.47; P<0.001) and large-for-gestational-age infants (8.6% vs. 22.4%; odds ratio, 0.33; 95% CI, 0.24 to 0.44; P<0.001). In contrast, they were associated with a higher risk of small-for-gestational-age infants (15.6% vs. 7.6%; odds ratio, 2.20; 95% CI, 1.64 to 2.95; P<0.001) and shorter gestation (273.0 vs. 277.5 days; mean difference −4.5 days; 95% CI, −2.9 to −6.0; P<0.001), although the risk of preterm birth was not significantly different (10.0% vs. 7.5%; odds ratio, 1.28; 95% CI, 0.92 to 1.78; P=0.15). The risk of stillbirth or neonatal death was 1.7% versus 0.7% (odds ratio, 2.39; 95% CI, 0.98 to 5.85; P=0.06). There was no significant between-group difference in the frequency of congenital malformations.

CONCLUSIONS
Bariatric surgery was associated with reduced risks of gestational diabetes and excessive fetal growth, shorter gestation, an increased risk of small-for-gestational-age infants, and possibly increased mortality. (Funded by the Swedish Research Council and others.)

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In 2008, an estimated 300 million women worldwide were obese (body-mass index [BMI; the weight in kilograms divided by the square of the height in meters], ≥30).[1] In 2011–2012 in the United States, 36% of adult women were obese,[2] and the majority of women in early pregnancy were either overweight or obese (BMI, ≥25).[3]

Maternal obesity is a risk factor for gestational diabetes, with attendant increased risks of macrosomia, delivery complications, obesity in the offspring, and later development of type 2 diabetes in the mother.[4-6] Maternal obesity is also associated with an increased risk of stillbirth,[7] preterm birth,[8] and some congenital malformations[9] and a reduced risk of infants born small for gestational age.[7]

Among obese persons with type 2 diabetes, bariatric surgery results in higher rates of short-term[10,11] and long-term[12,13] diabetes remission and prevention of incident diabetes than does conventional therapy for obesity.[14] The effect of prepregnancy bariatric surgery on gestational diabetes has been investigated in small studies with inconclusive results, and the majority of studies have not taken presurgery BMI into account.[15,16] Similarly, although systematic reviews have concluded that the risks of neonatal complications may be lower after bariatric surgery, this conclusion is based on studies with small sample sizes, heterogeneous study designs, and lack of matching for presurgery BMI.[15,16]

We therefore conducted a population-based study using data from nationwide Swedish registries, including information on presurgery BMI among women who had undergone bariatric surgery. We investigated the risks of gestational diabetes and adverse perinatal outcomes among women with a history of bariatric surgery as compared with women without such a history but with similar characteristics.

METHODS

STUDY DESIGN AND DATA SOURCES

In Sweden, prenatal care and delivery care are tax-funded, and the participation rate in the prenatal care program is almost 100%. The first prenatal visit commonly takes place at the end of the first trimester.[17] The Swedish Medical Birth Register includes information on more than 98% of all births in Sweden since 1973. Information is prospectively collected from standardized prenatal, obstetrical, and neonatal records.[18]

With the use of the unique personal identification number assigned to each Swedish resident,[19] we linked data from the Medical Birth Register to the National Patient Register, the Scandinavian Obesity Surgery Registry (SOReg), the Prescribed Drug Register, and the Education Register. The study was approved by the regional ethics committee at Karolinska Institutet, Stockholm.

The National Patient Register includes diagnostic and surgical information on hospital admissions and non–primary care outpatient visits, coded according to the Swedish versions of the *International Classification of Diseases, 10th revision* (ICD-10-SE) (for diagnostic information), and the *Classification of Surgical Procedures* (Nordic Medico-Statistical Committee) (for surgical information). SOReg was established nationwide in 2007; local data from a few hospitals were available beginning in 2004. The registry covers approximately 98.5% of all bariatric procedures in Sweden and includes presurgery and follow-up information. The nationwide Prescribed Drug Register was established in 2005 and includes all dispensed prescription drugs classified according to the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system. The Swedish Education Register includes information about the number of years of formal education.

INTERVENTION COHORT

Between 2006 and 2011, there were 651,561 deliveries recorded in the Swedish Medical Birth Register. We excluded multiple-birth pregnancies (since they are associated with a higher occurrence of complications and differences in fetal growth[20]) and women without a valid personal identification number at the time of delivery, who could therefore not be linked to other registries. After these exclusions, 628,778 singleton pregnancies remained, of which 1755 were in women who had undergone bariatric surgery between 1983 and 2011. Of these pregnancies, 670 occurred in women who had undergone bariatric surgery between 2004 and 2011, whose data were included in SOReg, and whose data on presurgery BMI were available (Fig. 1). From SOReg, we recorded the date of bariatric surgery, so that we could calculate the time between bariatric surgery

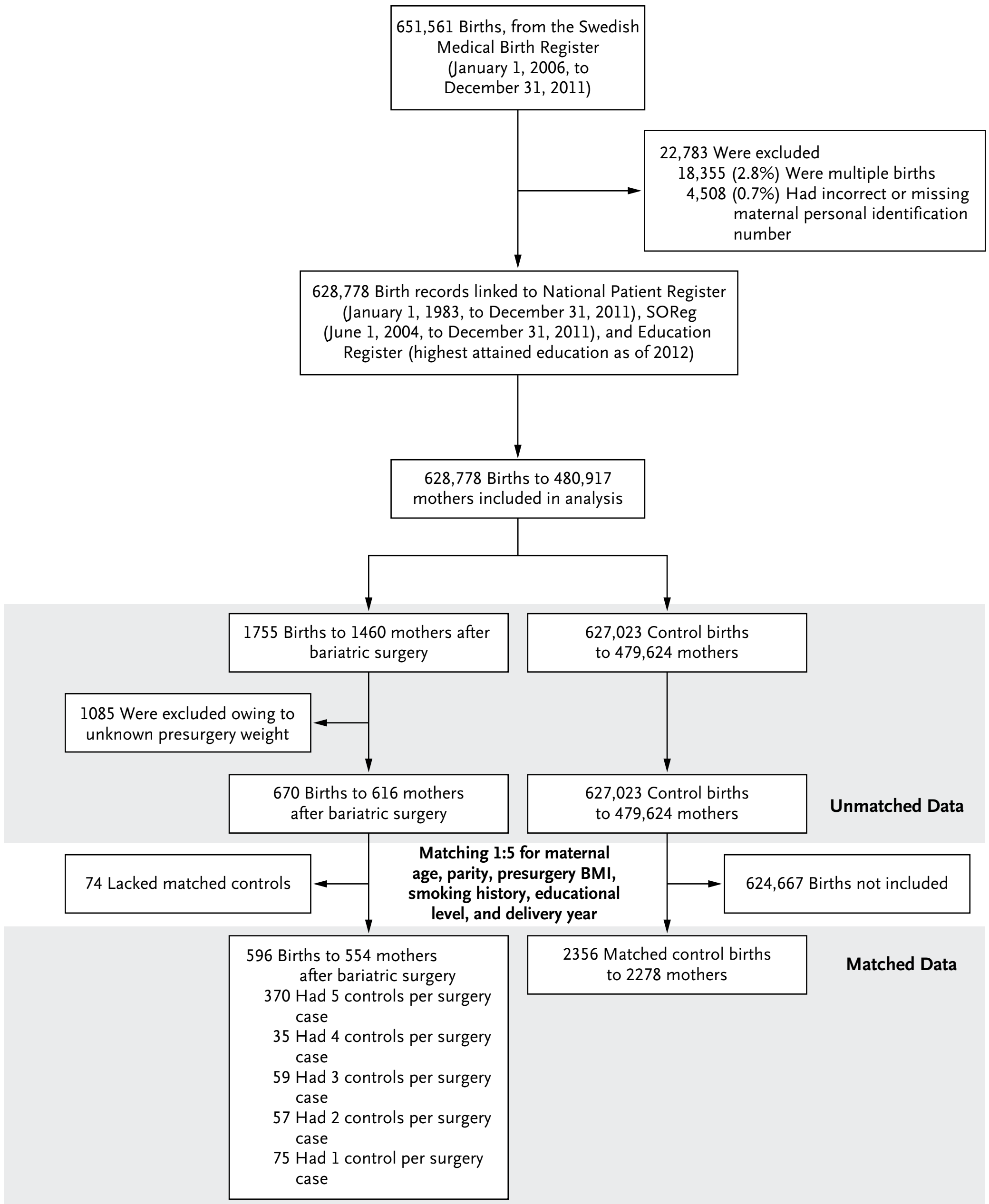


Figure 1. Identification of the Study Population and the Matched Control Population.

The exclusions for multiple births and incorrect or missing maternal personal identification numbers do not sum to 22,783 because there were 80 exclusions for both a multiple birth and an incorrect or missing maternal personal identification number. BMI denotes body-mass index, and SOReg Scandinavian Obesity Surgery Registry.

and delivery, and the type of the most recent procedure (6% of women underwent reoperation). (Surgery codes are provided in Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org.)

CONTROL COHORT

We created a matched control cohort composed of pregnancies in women without a history of bariatric surgery. Up to five control pregnancies were matched without replacement to each postsurgery pregnancy; once a pregnancy in a woman without a history of bariatric surgery was selected as a control, the same pregnancy could not be used as a control again. The matching factors were age (within 1 year older or younger), parity (nulliparous or parous), presurgery BMI (defined as presurgery BMI in the bariatric-surgery cohort and BMI during early pregnancy [i.e., at the first prenatal visit] in the control cohort; 30 to 34.9, 35 to 39.9, 40 to 44.9, 45 to 49.9, or ≥50), early-pregnancy smoking status (nonsmoker, smoker of 1 to 9 cigarettes per day, or smoker of ≥10 cigarettes per day, or missing data), educational level (≤9 years, 10 to 12 years, >12 years, or missing data), and delivery year (2006 to 2011).

COVARIATES

Weight and height measurements at the time of surgery were used to calculate presurgery BMI. Measured weight and self-reported height at the first prenatal visit were used to calculate early-pregnancy BMI; at that time, self-reported smoking status was also recorded. Data on maternal educational level and the mother's region of birth (Nordic [Sweden, Denmark, Norway, Finland, and Iceland] or non-Nordic) were retrieved and linked to data from other registries. A history of hospitalization for coexisting psychiatric, cardiovascular, or respiratory conditions (ICD-10 chapters V, IX, and X, respectively) and of substance abuse (ICD-10 codes F10 through F19) was identified with the use of the National Patient Register. In a subgroup of women, we had information on weight at delivery and could calculate weight gain during pregnancy (from the first prenatal visit).

OUTCOMES

Gestational diabetes was identified by the ICD-10 code (O244) in the Medical Birth Register or the National Patient Register or by ATC code A10A (prescription of insulin during pregnancy) in the Prescribed Drug Register (ICD-10 and ATC codes are provided in Table S2 in the Supplementary Appendix). For analyses of gestational diabetes, we excluded women with a diagnosis of diabetes before pregnancy.

In Sweden, women generally undergo random testing of capillary blood glucose levels four to six times during pregnancy. Women with a plasma blood glucose level of 8.0 mmol per liter (144 mg per deciliter) or higher or women who belong to a risk group (e.g., women with obesity, previous gestational diabetes or macrosomia, or a family history of diabetes) undergo an oral glucose-tolerance test conducted with a loading dose of 75 g. The diagnosis of gestational diabetes is generally made (and was made in this study) on the basis of a 2-hour plasma glucose level of 10.0 mmol per liter (180 mg per deciliter) or higher during such a glucose-tolerance test (range among Swedish counties, 8.9 to 12.2 mmol per liter [160 to 220 mg per deciliter]) or a fasting plasma glucose level of 7.0 mmol per liter (126 mg per deciliter) or higher. If oral glucose-tolerance testing is deemed unsafe (e.g., owing to the risk of the dumping syndrome [i.e., rapid gastric emptying]), fasting glucose levels and preprandial and postprandial glucose values are assessed instead.

Large-for-gestational-age infants were defined as those with a birth weight greater than the 90th percentile for sex and gestational age, and small-for-gestational-age infants as those with a birth weight less than the 10th percentile.[21] Other outcomes included low birth weight (<2500 g), macrosomia (>4500 g), preterm birth (<37 completed weeks of gestation), stillbirth (fetal death at ≥22 completed weeks of gestation on or after July 1, 2008 [97% of pregnancies ending in fetal death] and at ≥28 weeks before July 1, 2008 [<3% of pregnancies ending in fetal death]), neonatal death (death before 28 days of life), and major congenital malformations detected during the first year of life (divided into two categories: all malformations and malformations excluding chromosomal abnormalities) (ICD-10 codes are provided in Table S3 in the Supplementary Appendix).

The number of weeks of gestation was determined by ultrasound examination or, if ultrasonography was unavailable, by the recorded date of the first day of the last menstrual period. Since 1990, Swedish women have been routinely offered an ultrasound examination, generally early in the second trimester, for the purpose of estimating the weeks of gestation; approximately 95% accept this offer.[22]

Information on large-for-gestational-age infants, small-for-gestational-age infants, preterm births, stillbirths, and neonatal deaths was derived from the Medical Birth Register. Major congenital malformations were identified from the Medical Birth Register and the National Patient Register (through the first year of life).

Table 1. Maternal Characteristics in Singleton Pregnancies in Sweden between 2006 and 2011.*

Characteristic	Before Matching			After Matching		
	Pregnancies after Bariatric Surgery (N=670)†	General-Population Pregnancies (N=627,023)‡	P Value	Pregnancies after Bariatric Surgery (N=596)†	Matched Control Pregnancies (N=2356)	P Value§
Surgery-to-delivery interval						
Mean — yr	2±1			2±1		
<1 Yr — no. (%)	47 (7.0)			42 (7.0)		
1 to <2 Yr — no. (%)	342 (51.0)			305 (51.2)		
2 to <5 Yr — no. (%)	279 (41.6)			247 (41.4)		
≥5 Yr — no. (%)	2 (0.3)			2 (0.3)		
Maternal age						
Mean — yr	31±5	30±5	<0.001	31±5	31±5	0.19
13–24 Yr — no. (%)	64 (9.6)	91,695 (14.6)	<0.001	57 (9.6)	221 (9.4)	0.64
25–29 Yr — no. (%)	197 (29.4)	180,274 (28.8)	<0.001	182 (30.5)	744 (31.6)	0.64
30–34 Yr — no. (%)	222 (33.1)	218,441 (34.8)	<0.001	195 (32.7)	779 (33.1)	0.64
≥35 Yr — no. (%)	187 (27.9)	136,610 (21.8)	<0.001	162 (27.2)	612 (26.0)	0.64
BMI						
Before surgery						
Mean	44.5±5.8			43.7±5.4	41.8±4.8	<0.001¶
30.0–34.9 — no. (%)	15 (2.2)			15 (2.5)	75 (3.2)	NA
35.0–39.9 — no. (%)	126 (18.8)			126 (21.1)	611 (25.9)	NA
40.0–44.9 — no. (%)	262 (39.1)			250 (41.9)	1162 (49.3)	NA
45.0–49.9 — no. (%)	149 (22.2)			127 (21.3)	394 (16.7)	NA
≥50 — no. (%)	118 (17.6)			78 (13.1)	114 (4.8)	NA
In early pregnancy‖						
Mean	30.6±5.2	24.6±4.6	<0.001	30.3±4.9	41.8±4.8	<0.001
<18.5 — no. (%)	1 (0.1)	14,044 (2.2)	<0.001	1 (0.2)	0	<0.001
18.5–24.9 — no. (%)	77 (11.5)	350,573 (55.9)	<0.001	75 (12.6)	0	<0.001
25.0–29.9 — no. (%)	249 (37.2)	142,015 (22.6)	<0.001	230 (38.6)	0	<0.001
30.0–34.9 — no. (%)	194 (29.0)	48,195 (7.7)	<0.001	176 (29.5)	75 (3.2)	<0.001
35.0–39.9 — no. (%)	79 (11.8)	14,834 (2.4)	<0.001	65 (10.9)	611 (25.9)	<0.001
≥40 — no. (%)	42 (6.3)	5476 (0.9)	<0.001	30 (5.0)	1670 (70.9)	<0.001
Mean change in weight and BMI from surgery to early pregnancy**						
Weight loss — kg	38±13			37±12		
Decrease in BMI — units	13.8±4.5			13.4±4.3		
Smoking status — no. (%)††						
Nonsmoker	543 (81.0)	560,059 (89.3)	<0.001	513 (86.1)	2064 (87.6)	NA
1–9 Cigarettes per day	75 (11.2)	31,525 (5.0)	<0.001	59 (9.9)	214 (9.1)	NA
≥10 Cigarettes per day	40 (6.0)	9401 (1.5)	<0.001	22 (3.7)	75 (3.2)	NA
Educational level — no. (%)‡‡						
≤9 Yr	126 (18.8)	66,246 (10.6)	<0.001	103 (17.3)	378 (16.0)	NA
10–12 Yr	408 (60.9)	237,712 (37.9)	<0.001	368 (61.7)	1432 (60.8)	NA
>12 Yr	133 (19.9)	306,314 (48.9)	<0.001	122 (20.5)	533 (22.6)	NA

Table 1. (Continued.)

Characteristic	Before Matching			After Matching		
	Pregnancies after Bariatric Surgery (N=670)†	General-Population Pregnancies (N=627,023)‡	P Value	Pregnancies after Bariatric Surgery (N=596)†	Matched Control Pregnancies (N=2356)	P Value§
Nulliparous — no. (%)	280 (41.8)	281,705 (44.9)	<0.001	238 (39.9)	900 (38.2)	NA
Coexisting conditions before pregnancy — no. (%)						
Diabetes	20 (3.0)	4802 (0.8)	<0.001	18 (3.0)§§	62 (2.6)§§	0.62
Cardiovascular disease	21 (3.1)	6216 (1.0)	<0.001	17 (2.9)	38 (1.6)	0.12
Respiratory disease	79 (11.8)	23,359 (3.7)	<0.001	71 (11.9)	172 (7.3)	<0.001
Psychiatric disease	72 (10.7)	21,747 (3.5)	<0.001	62 (10.4)	130 (5.5)	<0.001
Substance abuse	9 (1.3)	2571 (0.4)	<0.001	9 (1.5)	10 (0.4)	<0.001

* Plus–minus values are means ±SD. The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters. NA denotes not applicable (P=1.0 for all comparisons of categorical matching factors).
† Data on presurgery weight were obtained from the Scandinavian Obesity Surgery Registry (SOReg).
‡ General-population pregnancies were those in women with no history of bariatric surgery.
§ Comparisons of continuous variables were performed with the use of two-way analysis of variance, and comparisons of categorical variables were performed with the use of conditional logistic regression (both conditioned on the matching set).
¶ The mean between-group difference in BMI (mean difference, 0.47; 95% confidence interval, 0.34 to 0.63) was conditioned on the matching set. The matching was performed according to BMI categories; hence, mean BMI in each BMI category was slightly higher in the bariatric-surgery group.
‖ BMI data were missing for 28 women in the bariatric-surgery cohort before matching and 51,886 women in the general population, as well as 19 women in the bariatric-surgery cohort and no women in the control cohort after matching.
** Data on early-pregnancy weight and BMI were missing for 28 women in the bariatric-surgery cohort before matching and 19 women in the bariatric-surgery cohort after matching.
†† Data on early-pregnancy smoking status were missing for 12 women in the bariatric-surgery cohort before matching and 26,038 women in the general population, as well as 2 women in the bariatric-surgery cohort and 3 women in the control cohort after matching.
‡‡ Data on education were missing for 3 women in the bariatric-surgery cohort before matching and 16,751 women in the general population, as well as 3 women in the bariatric-surgery cohort and 13 women in the control cohort after matching.
§§ Women with prepregnancy diabetes were excluded from analyses of gestational diabetes.

STATISTICAL ANALYSIS

Singleton pregnancies in women with a history of bariatric surgery were compared with matched controls (singleton pregnancies in women without a history of bariatric surgery). We estimated odds ratios for postsurgery pregnancies versus control pregnancies with the use of logistic regression conditioned on the matching set, with each set consisting of one pregnancy after bariatric surgery and up to five matched control pregnancies. Adjustments were made for a history of hospitalization of the mother for coexisting psychiatric, cardiovascular, or respiratory conditions, as well as for a history of substance abuse and for the mother's country of birth.

These analyses were performed on individual pregnancies, which made it possible for a woman to contribute more than one pregnancy; therefore, risk estimation was also performed by the generalized-estimating-equation method (with the mother's identification as a cluster and assuming an exchangeable correlation structure), with adjustment for the possible dependence in outcome that could be introduced by having repeated pregnancies in the same mother. In another sensitivity analysis, we restricted inclusion to one pregnancy per woman (and therefore excluded 42 postsurgery pregnancies and 238 control pregnancies).

To assess the homogeneity of effects, we tested for interactions between bariatric-surgery status (surgery or no surgery) and parity (nulliparous or multiparous), as well as presurgery BMI, the interval from surgery to delivery, and the decrease in BMI from presurgery to early pregnancy (at or above vs. below the median levels for all three subgroups). The effect of weight gain during pregnancy was assessed in the subgroup of women for whom data on weight gain were available.

Data were analyzed with the use of SAS software, version 9.4 (SAS Institute). Two-sided P values of less than 0.05 were considered to indicate statistical significance. No adjustment was made for multiple comparisons.

RESULTS

PARTICIPANT CHARACTERISTICS

As compared with pregnant women in the general population, women in the bariatric-surgery cohort were older, had lower educational levels, and were more likely to be obese, to smoke, and to be multiparous (P<0.001 for all comparisons) (Table 1). These differences were eliminated by the matching procedure, in which controls were identified for all but 74 (11%) of the 670 postsurgery pregnancies. In analyses of the matched cohorts, women with a history of bariatric surgery, as compared with women in the control cohort, had a slightly but significantly higher mean presurgery BMI (mean between-group difference in BMI, 0.5) and a history of more hospitalizations for cardiovascular, respiratory, or psychiatric disease and of more substance abuse (Table 1).

Nearly 98% (582) of the bariatric-surgery procedures were gastric bypass, 2% (11) were gastric banding, and less than 1% (3) were another procedure. Of the women who underwent bariatric surgery, 14% had a history of diabetes before surgery. The median interval from surgery to delivery was 1.8 years (interquartile range, 1.4 to 2.5). The mean presurgery BMI was 43.7, and the mean weight loss between surgery and early pregnancy was 37 kg (mean decrease in BMI, 13.4) (Table 1, and Fig. S1 in the Supplementary Appendix).

OUTCOMES

Gestational Diabetes

Gestational diabetes was diagnosed in 1.9% of the postsurgery pregnancies and in 6.8% of the control pregnancies (odds ratio 0.25; 95% confidence interval [CI], 0.13 to 0.47; P<0.001; Table 2). Among women for whom information on the date of diagnosis of gestational diabetes was available (9 of 11 [82%] in the bariatric-surgery group and 134 of 157 [85%] in the control group), the median time of gestation at which the diagnosis was made was 32 weeks in both groups.

Birth Weight and Related Measures

Postsurgery pregnancies, as compared with control pregnancies, were associated with a lower risk of large-for-gestational-age infants (8.6% vs. 22.4%; odds ratio, 0.33; 95% CI, 0.24 to 0.44; P<0.001) and of macrosomia (1.2% vs. 9.5%; odds ratio, 0.11; 95% CI, 0.05 to 0.24; P<0.001) (Table 2). However, postsurgery pregnancies were associated with an increased risk of small-for-gestational-age infants (15.6% vs. 7.6%; odds ratio, 2.20; 95% CI, 1.64 to 2.95; P<0.001) and a nonsignificantly increased risk of low-birth-weight infants (6.8% vs. 4.5%; odds ratio, 1.34; 95% CI, 0.88 to 2.04; P=0.17) (Table 2).

Preterm Birth, Congenital Malformations, and Mortality

Although postsurgery pregnancies, on average, had a shorter gestation than did control pregnancies (273.0 days vs. 277.5 days; mean difference, −4.5 days; 95% CI, −2.9 to −6.0; P<0.001), the risk of preterm birth did not differ significantly between the groups (10.0% vs. 7.5%; odds ratio, 1.28; 95% CI, 0.92 to 1.78; P=0.15). The risk of the combined outcome of stillbirth or neonatal death was 1.7% in the postsurgery group and 0.7% in the control group (odds ratio, 2.39; 95% CI, 0.98 to 5.85; P=0.06). There was no significant between-group difference in the frequency of congenital malformations (Table 2).

SUBGROUP ANALYSES

In the four interaction tests, we found no significant effect modification of bariatric surgery on gestational diabetes according to presurgery BMI, the interval from surgery to delivery, or the magnitude of reduction in BMI from presurgery to early pregnancy (at or above vs. below the median levels for all three subgroups) or according to parity (nulliparous or multiparous) (Fig. 2). There was also no significant effect modification of bariatric surgery on perinatal outcomes, except in 3 of the 16 interaction tests, which yielded the following significant interactions: a greater decrease in BMI was associated with a lower risk of large-for-gestational-age infants and a higher risk of preterm birth, and a longer surgery-to-delivery interval was associated with a higher risk of small-for-gestational-age infants (Fig. 2).

SENSITIVITY ANALYSES

Data about weight gain during pregnancy were available for 33% of postsurgery pregnancies (219 of 670) and 33% of control pregnancies (209,265 of 627,023). Weight gain was similar in the two groups of women (8.8 kg in the postsurgery-pregnancy group and 9.0 kg in the control-pregnancy group; mean difference, −0.2 kg; 95% CI, −1.1 to 1.4; P=0.77). Adjustment for weight gain during pregnancy did not materially affect

Table 2. Gestational Diabetes and Perinatal Outcomes among Women with and Those without a History of Bariatric Surgery.

Variable	Bariatric-Surgery Group (N=596)	Matched Control Group (N=2356)	Risk Difference	Odds Ratio (95% CI)*	P Value
	no./total no. (%)		*percentage points (95% CI)*		
Gestational diabetes†					
Total	11/578 (1.9)	157/2294 (6.8)	−4.9 (−6.5 to −3.4)	0.25 (0.13 to 0.47)	<0.001
Insulin-treated	4/578 (0.7)	83/2294 (3.6)	−2.9 (−3.9 to −1.9)	0.17 (0.06 to 0.49)	<0.001
Large-for-gestational-age infant‡	51/590 (8.6)	523/2336 (22.4)	−13.8 (−16.6 to −11.0)	0.33 (0.24 to 0.44)	<0.001
Macrosomia‡	7/590 (1.2)	221/2336 (9.5)	−8.3 (−9.7 to −6.8)	0.11 (0.05 to 0.24)	<0.001
Small-for-gestational-age infant‡	92/590 (15.6)	178/2336 (7.6)	8.0 (4.8 to 11.1)	2.20 (1.64 to 2.95)	<0.001
Low-birth-weight infant‡	40/590 (6.8)	105/2336 (4.5)	2.3 (0.1 to 4.5)	1.34 (0.88 to 2.04)	0.17
Preterm birth§	59/590 (10.0)	176/2344 (7.5)	2.5 (−0.2 to 5.1)	1.28 (0.92 to 1.78)	0.15
Stillbirth¶	6/596 (1.0)	12/2356 (0.5)	0.5 (−0.4 to 1.3)	1.89 (0.59 to 6.05)	0.28
Neonatal death <28 days after live birth§	4/590 (0.7)	5/2344 (0.2)	0.5 (−0.2 to 1.2)	2.93 (0.57 to 15.14)	0.20
Stillbirth or neonatal death	10/596 (1.7)	17/2356 (0.7)	1.0 (−0.1 to 2.0)	2.39 (0.98 to 5.85)	0.06
Major congenital malformations§					
Total	14/590 (2.4)	83/2344 (3.5)	−1.2 (−2.6 to 0.3)	0.72 (0.40 to 1.29)	0.27
Excluding chromosomal abnormalities§	12/590 (2.0)	79/2344 (3.4)	−1.3 (−2.7 to 0.0)	0.63 (0.34 to 1.18)	0.16

* Odds ratios were conditioned on the matching set, including one pregnancy after bariatric surgery and up to five controls, with matching for maternal age, parity, presurgery BMI (with the use of early-pregnancy BMI in the controls), smoking, educational level, and delivery year; adjustments were made for history of coexisting conditions, history of substance abuse, and mother's country of birth.

† Analyses of gestational diabetes excluded women with prepregnancy diabetes (18 women [3%] in the bariatric-surgery cohort and 62 women [3%] in the matched control cohort).

‡ Analyses of large-for-gestational-age infants (>90th percentile), small-for-gestational-age infants (<10th percentile), macrosomia (birth weight >4500 g), and low birth weight (<2500 g) excluded stillbirths and births without data on birth weight. Analyses of large-for-gestational-age infants and small-for-gestational-age infants also excluded births without data on gestational age. There were 6 exclusions in the bariatric-surgery group (1.0%) and 20 in the matched-control group (0.9%).

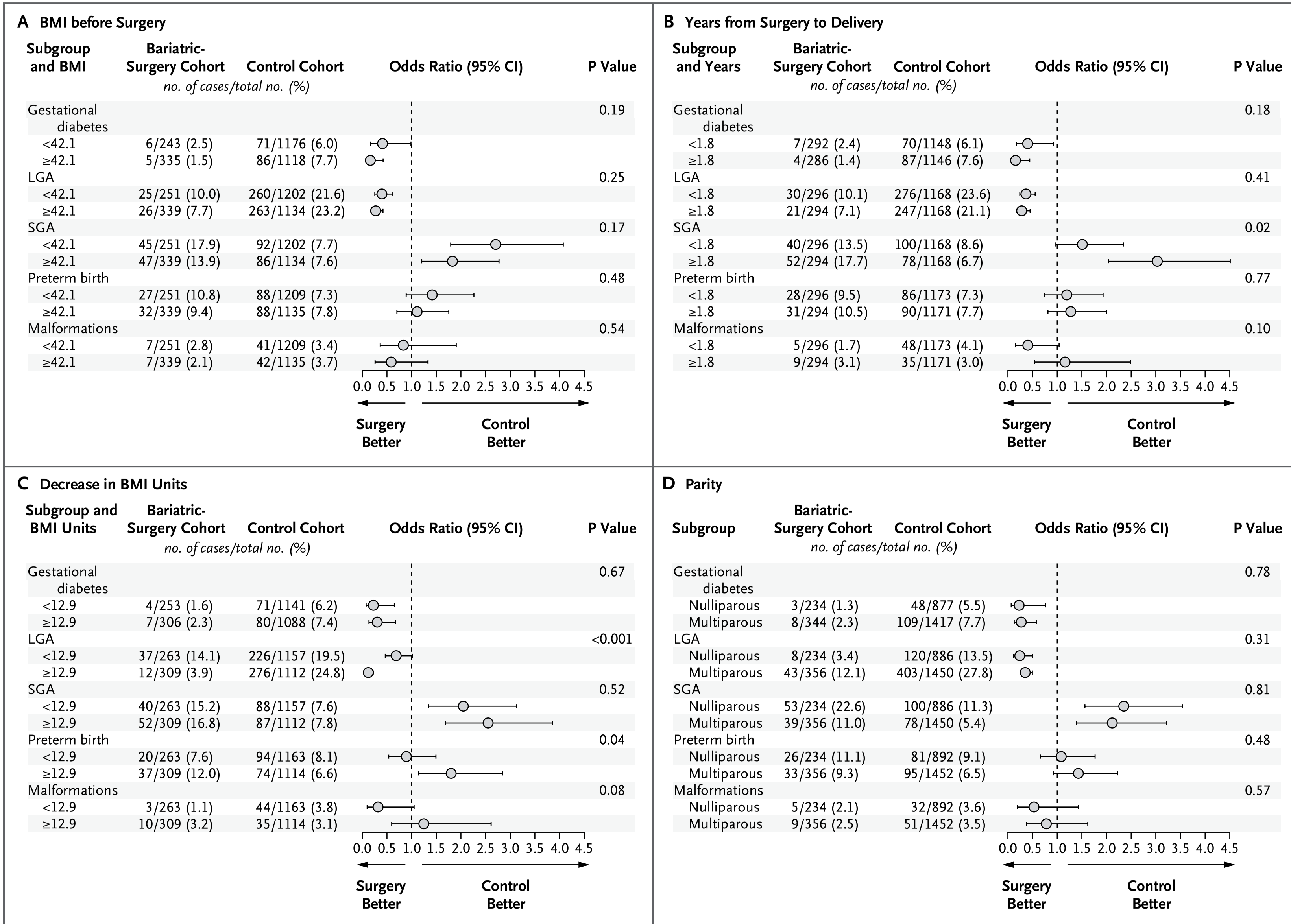
§ Analyses of preterm birth, neonatal death, and congenital malformations excluded stillbirths and births without data on gestational age. There were 6 exclusions in the bariatric-surgery group (1.0%) and 12 in the matched-control group (0.5%).

¶ Stillbirth was defined as fetal death at 22 or more completed weeks of gestation on or after July 1, 2008 (97% of pregnancies), and at 28 or more weeks before July 1, 2008 (<3% of pregnancies).

the association between bariatric surgery and any of the outcomes (Table S4 in the Supplementary Appendix). Results were similar in analyses that included only one pregnancy per woman after bariatric surgery (Table S5 in the Supplementary Appendix) and in analyses with the use of a generalized-estimation-equation framework (adjusted for, instead of conditioned on, the matching factors) (Table S6 in the Supplementary Appendix).

DISCUSSION

In this nationwide prospective cohort study, women with a history of bariatric surgery had a lower risk of gestational diabetes and large-for-gestational-age infants and an increased risk of small-for-gestational-age infants and a shorter gestation than did women in a control group matched for presurgery BMI (with the use of early-pregnancy BMI in the control cohort). Previous studies have reported conflicting results regarding the effect of bariatric surgery on the development of gestational diabetes; these inconsistencies are most likely explained by small sample sizes and heterogeneous study designs.[15,16] In one previous study[23] in which, as in the present study, cases were matched to controls according to presurgery BMI, there were no cases of gestational diabetes among 70 women who had a history of bariatric surgery and 21 cases among 140 matched controls; in our cohort, gestational diabetes was diagnosed in 1.9% of the women who had undergone bariatric surgery and in 6.8% of matched controls. The previous study also reported perinatal mortality of



A BMI before Surgery

Subgroup and BMI	Bariatric-Surgery Cohort (no. of cases/total no. (%))	Control Cohort (no. of cases/total no. (%))	P Value
Gestational diabetes			0.19
<42.1	6/243 (2.5)	71/1176 (6.0)	
≥42.1	5/335 (1.5)	86/1118 (7.7)	
LGA			0.25
<42.1	25/251 (10.0)	260/1202 (21.6)	
≥42.1	26/339 (7.7)	263/1134 (23.2)	
SGA			0.17
<42.1	45/251 (17.9)	92/1202 (7.7)	
≥42.1	47/339 (13.9)	86/1134 (7.6)	
Preterm birth			0.48
<42.1	27/251 (10.8)	88/1209 (7.3)	
≥42.1	32/339 (9.4)	88/1135 (7.8)	
Malformations			0.54
<42.1	7/251 (2.8)	41/1209 (3.4)	
≥42.1	7/339 (2.1)	42/1135 (3.7)	

B Years from Surgery to Delivery

Subgroup and Years	Bariatric-Surgery Cohort (no. of cases/total no. (%))	Control Cohort (no. of cases/total no. (%))	P Value
Gestational diabetes			0.18
<1.8	7/292 (2.4)	70/1148 (6.1)	
≥1.8	4/286 (1.4)	87/1146 (7.6)	
LGA			0.41
<1.8	30/296 (10.1)	276/1168 (23.6)	
≥1.8	21/294 (7.1)	247/1168 (21.1)	
SGA			0.02
<1.8	40/296 (13.5)	100/1168 (8.6)	
≥1.8	52/294 (17.7)	78/1168 (6.7)	
Preterm birth			0.77
<1.8	28/296 (9.5)	86/1173 (7.3)	
≥1.8	31/294 (10.5)	90/1171 (7.7)	
Malformations			0.10
<1.8	5/296 (1.7)	48/1173 (4.1)	
≥1.8	9/294 (3.1)	35/1171 (3.0)	

C Decrease in BMI Units

Subgroup and BMI Units	Bariatric-Surgery Cohort (no. of cases/total no. (%))	Control Cohort (no. of cases/total no. (%))	P Value
Gestational diabetes			0.67
<12.9	4/253 (1.6)	71/1141 (6.2)	
≥12.9	7/306 (2.3)	80/1088 (7.4)	
LGA			<0.001
<12.9	37/263 (14.1)	226/1157 (19.5)	
≥12.9	12/309 (3.9)	276/1112 (24.8)	
SGA			0.52
<12.9	40/263 (15.2)	88/1157 (7.6)	
≥12.9	52/309 (16.8)	87/1112 (7.8)	
Preterm birth			0.04
<12.9	20/263 (7.6)	94/1163 (8.1)	
≥12.9	37/309 (12.0)	74/1114 (6.6)	
Malformations			0.08
<12.9	3/263 (1.1)	44/1163 (3.8)	
≥12.9	10/309 (3.2)	35/1114 (3.1)	

D Parity

Subgroup	Bariatric-Surgery Cohort (no. of cases/total no. (%))	Control Cohort (no. of cases/total no. (%))	P Value
Gestational diabetes			0.78
Nulliparous	3/234 (1.3)	48/877 (5.5)	
Multiparous	8/344 (2.3)	109/1417 (7.7)	
LGA			0.31
Nulliparous	8/234 (3.4)	120/886 (13.5)	
Multiparous	43/356 (12.1)	403/1450 (27.8)	
SGA			0.81
Nulliparous	53/234 (22.6)	100/886 (11.3)	
Multiparous	39/356 (11.0)	78/1450 (5.4)	
Preterm birth			0.48
Nulliparous	26/234 (11.1)	81/892 (9.1)	
Multiparous	33/356 (9.3)	95/1452 (6.5)	
Malformations			0.57
Nulliparous	5/234 (2.1)	32/892 (3.6)	
Multiparous	9/356 (2.5)	51/1452 (3.5)	

Figure 2 (facing page). Odds Ratios for Gestational Diabetes and Adverse Perinatal Outcomes According to Presurgery BMI, Surgery-to-Delivery Interval, Change in BMI, and Parity in the Bariatric-Surgery Cohort versus the Control Cohort.

Odds ratios were estimated with the use of logistic regression conditioned on the matching set (one pregnancy after bariatric surgery and up to five controls matched for maternal age, parity, presurgery body-mass index [BMI], early-pregnancy smoking status, educational level, and year of delivery) and adjusted for history of coexisting conditions, history of substance abuse, and mother's country of birth. LGA denotes large for gestational age, and SGA small for gestational age.

5.7% among pregnancies in women with a history of bariatric surgery and a rate of 0.7% among the control pregnancies. Similarly, in our study, we noted a higher risk of the combined outcome of stillbirth or neonatal death among women with a history of bariatric surgery than in the controls (1.7% vs. 0.7%), although such events were uncommon and the difference was of borderline significance (P=0.06).

We also found that women who had undergone bariatric surgery had a lower risk of delivering large-for-gestational-age infants but a higher risk of delivering small-for-gestational-age infants. Overall, they did not have a significantly higher risk of preterm birth, but subgroup analyses suggested that this risk may be increased among women with a greater decrease in BMI between surgery and early pregnancy. Similar associations were reported from two cohort studies in which cases and controls were matched for early-pregnancy BMI, although such a design addresses a different research question than does the current study.[24,25] The between-group difference in fetal growth was expected, given that the women with a history of bariatric surgery had, on average, a decrease in weight of 37 kg (decrease in BMI, 13) after surgery. However, given the direct association between BMI and the risk of preterm birth,[8] we expected that the risk of preterm birth would be lower, rather than higher, after bariatric surgery. Our study showed a median surgery-to-conception interval of 1.1 years, which suggested that many women may have been continuing to lose weight when they became pregnant. Continued weight loss may affect fetal nutrition and could influence the risk of preterm birth.

Despite known adverse effects of gastric bypass surgery on the metabolism of iron, vitamin B_{12}, and folate,[26] we found no significant effect of bariatric surgery on the overall risk of congenital malformations. Still, we cannot exclude the possibility that risks of specific malformations differed between the groups.

Although this nationwide study is, to our knowledge, the largest study to date comparing pregnancy outcomes between women with and those without a history of bariatric surgery, with matching for presurgery BMI, limitations of the study must be considered. The matching for presurgery BMI and adjustment for other factors was intended to identify independent effects of bariatric surgery on pregnancy outcomes, but the observational design of the study makes it impossible to determine cause and effect. There may be residual confounding, because women who undergo surgery may have differed from women in the control cohort with respect to other factors not accounted for in the analyses. Also, there is a possibility of chance findings, since we investigated multiple outcomes.

Another potential limitation is selection bias. For example, with regard to prepregnancy diabetes status, women with a history of bariatric surgery may be followed more closely than women in the control cohort with similar characteristics. If women with unrecognized preexisting diabetes were overrepresented in the control group, this could lead to bias toward a lower risk of gestational diabetes in the bariatric-surgery group as compared with the control group. However, all pregnant women undergo glucose screenings starting at their first maternity care visit, and obese women commonly undergo oral glucose-tolerance testing, since they are regarded as a high-risk group. Also, the majority of the diagnoses of gestational diabetes were ascertained at approximately week 30, and it is unlikely that prevalent type 2 diabetes would go undetected for so long.

In addition, it is likely that some women with a history of bariatric surgery were infertile before surgery, whereas the control cohort consisted of a selected group of obese women who were able to conceive. The slightly lower BMI and rates of previous hospitalizations for respiratory and psychiatric coexisting conditions and of substance abuse in the control group suggest that this group may have been a healthier group overall.

Because the Swedish population is mostly white, our findings cannot necessarily be generalized to other races. In addition, our sample had a median surgery-to-conception interval of 1.1 years and a maximum of 4.3 years and may not be generalizable to pregnancies with longer surgery-to-conception intervals. Also, 98% of all procedures were gastric bypass surgery, and it is not known whether our results apply to other bariatric procedures.

In conclusion, this nationwide cohort study showed that a history of bariatric surgery was associated with reduced risks of gestational diabetes and large-for-gestational-age infants. However, increased surveillance during pregnancy and the neonatal period is warranted, since a history of bariatric surgery was also associated with small-for-gestational-age infants, a shorter length of gestation, and potentially an increased risk of stillbirth or neonatal death.

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REVIEW Open Access

Pregnancy after bariatric surgery: a narrative literature review and discussion of impact on pregnancy management and outcome

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Abstract

Bariatric surgery (BS) is regarded to be the most effective treatment of obesity with long lasting beneficial effects including weight loss and improvement of metabolic disorders. A considerable number of women undergoing BS are at childbearing age.

Although the surgery mediated weight loss has a positive effect on pregnancy outcome, the procedures might be associated with adverse outcomes as well, for example micronutrient deficiencies, iron or B12 deficiency anemia, dumping syndrome, surgical complications such as internal hernias, and small for gestational age (SGA) offspring, possibly due to maternal undernutrition. Also, there is no international consensus concerning the ideal time to conception after BS. Hence, the present narrative review intents to summarize the available literature concerning the most common challenges which arise before and during pregnancy after BS, such as fertility related considerations, vitamin and nutritional deficiencies and their adequate compensation through supplementation, altered glucose metabolism and its implications for gestational diabetes screening, the symptoms and treatment of dumping syndrome, surgical complications and the impact of BS on pregnancy outcome. The impact of different bariatric procedures on pregnancy and fetal outcome will also be discussed, as well as general considerations concerning the monitoring and management of pregnancies after BS.

Whereas BS leads to the mitigation of many obesity-related pregnancy complications, such as gestational diabetes mellitus (GDM), pregnancy induced hypertension and fetal macrosomia; those procedures pose new risks which might lead to adverse outcomes for mothers and offspring, for example nutritional deficiencies, anemia, altered maternal glucose metabolism and small for gestational age children.

Keywords: Bariatric surgery, Pregnancy outcome, Pregnancy management, Narrative review

Background

There is a dramatic increase in overweight and obesity worldwide. The WHO estimates that 39% of adults worldwide are overweight (BMI ≥ 25 kg/m^2) and 13% are obese (BMI ≥30 kg/m^2) [1]. It is widely known that obesity is associated with numerous comorbidities such as hypertension, musculoskeletal disorders, cancer and type 2 diabetes [1–3]. Likewise, overweight or obese pregnant women show an increased risk for gestational diabetes [4], pre-eclampsia [5], spontaneous miscarriage [6], large for gestational age offspring and even fetal (neurological and cardiovascular) malformations [7]. Children from obese mothers may also develop health complications in later life, such as hypertension, diabetes or cardiovascular disease, due to epigenetic changes [8].

Weight loss is associated with improved fertility rates and pregnancy outcomes, [9], with BS having proven to be the most effective treatment [10]. However, BS itself can be a risk factor for the development of adverse pregnancy outcomes and poses a challenge for obstetricians. In the following narrative review, we will give a comprehensive overview on the benefits and risks of BS on pregnancy

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outcomes, like risk of malnutrition, maternal anemia, development of internal hernia, reduced risk of gestational hypertension and GDM (Table 1) and higher risk of SGA outcomes (Table 2).

Overview of bariatric procedures

Surgical techniques

Bariatric surgery might be indicated if other attempts of losing weight have failed. It is the most effective way for weight loss and the reduction of comorbidities like type II diabetes mellitus [11] and hypertension [12] and has favourable effects on cardiac function [13, 14]. International guidelines stipulate that BS should be considered if a patient's BMI exceeds 40 kg/m^2, or in case of a BMI between 35 kg/m^2 and 40 kg/m^2 with associated severe comorbidities; in the case of coexisting diabetes mellitus even in the case of a BMI between 30 kg/m^2 and 35 kg/m^2 [3].

BS is divided into restrictive and malabsorptive procedures or a combination of both. The most widely used surgical procedures are the Roux-en-Y gastric bypass (RYGB), the sleeve gastrectomy and the adjustable gastric band. Other techniques such as the biliopancreatic diversion are not very common and will therefore not be discussed in this review. RYGB (Fig. 1a) is a combined malabsorptive and restrictive procedure which consists of a horizontal partitioning of the upper part of the stomach to create a gastric pouch. 75 to 150 cm of the small intestine are used to create the alimentary limb which carries ingested food to the bowel without the addiction of biliopancreatic secretions which are carried directly into the bowel through the biliopancreatic limb, typically 30 to 60 cm in length [15].

Sleeve gastrectomy (Fig. 1b) is a restrictive procedure and is performed as laparoscopic gastric resection which creates a small gastric pouch. It can be combined with the duodeno-ileostomy as part of a biliopancreatic bypass [15].

Adjustable gastric banding (Fig. 1c) is normally performed as a laparoscopic procedure (LAGB) and consists in placing a band 1 to 2 cm below the gastroesophageal junction, creating an upper gastric pouch with a capacity of 20 to 30 mL. The degree of constriction of the stomach can be adjusted by the introduction of saline through the port [15].

Other less frequent procedures, such as the biliopancreatic diversion, will not be discussed in this paper.

Less invasive endoscopic techniques

By the endoscopic placement of intragastric balloons with a volume of at least 400 ml gastric space is occupied and gastric motility is altered [16]. Compared to standard bariatric surgery, bariatric endoscopy (BE) is considered to be less invasive, more economic and associated with lower morbidity and mortality. Depending on individual circumstances, it might also be approved for patients with a BMI between 30 and 35 kg/m^2 [16, 17]. Furthermore, the procedure can be repeated if necessary [17]. Bariatric endoscopy is associated with beneficial metabolic effects like reduced incidence of hyperuricemia, hypertriglyceridemia, hypercholesterolemia and diabetes mellitus [18]. To our knowledge there is currently only one retrospective study that investigated if BE has potential benefits for patients with obesity-induced infertility. The authors showed that 15 out of 27 obese women conceived successfully after the placement of an intragastric balloon and subsequent weight loss. All pregnancies were uneventful and ended with life births; however, further research is needed before concluding that BE is safe in reproductive age and pregnancy [19].

Literature searching algorithm

The references for this review were obtained from Pubmed and MedLine databases using the MeSH Terms: "obesity", "bariatric surgery", "pregnancy and bariatric surgery", "obesity and fertility", "obesity and pharmacology", "obesity and bariatric surgery", "obesity and diabetes", "diabetes and pregnancy", "gestational diabetes and hypertension", "obesity and hypertension", "bariatric surgery and hypertension", "obesity and heart disease", "bariatric surgery and heart disease", "gastric bypass and anaemia", "gastric bypass and hyperparathyroidism", "bariatric surgery and vitamin D", "dietary supplements and gastric bypass", "gastric bypass and abdominal hernia", "fetal macrosomia", "infant, small for gestational age, breastfeeding and bariatric surgery". We prioritized longitudinal observational studies, cohort studies and meta-analysis. Furthermore, we used clinical guidelines from the American Congress of Obstetricians and Gynaecologists (ACOG) for the management of pregnancy and delivery after bariatric surgery and the Scientific Impact Paper on the role of bariatric surgery in improving reproductive health by the Royal College of Obstetricians and Gynaecologists.

Challenges and benefits of Bariatric Surgery before pregnancy

Although obesity has become a major health care problem within the last years along with increasing prevalence of BS in women of childbearing age, there is no international consensus about management of pregnancy after BS. Even though BS seems to reduce obesity-related fertility issues and adverse pregnancy outcomes [20–22], obstetricians have to consider pregnancy related complications possibly caused by BS [20, 23].

The standard recommendation of the ACOG for women wishing to conceive after BS is to delay pregnancy for at least 1 to 1.5 years after surgery [23], which is also supported by the obesity management task force of the European Association for the Study of Obesity

[24]. During the first post-surgical year a rapid weight loss is to be expected and becoming pregnant in this catabolic time frame could possibly lead to an altered nutritional supply to the growing fetus [21]. However, in contrast to these guidelines one recent study found no evidence supporting this recommendation [25].

Pregnancies after BS, especially malabsorptive procedures, are characterized by nutritional deficiencies such as anemia, low protein and vitamin levels [26, 27]. Furthermore, a history of BS is associated with altered glucose metabolism, impacting the diagnosis of hyperglycemia [28]. Recent data also indicates a higher risk for SGA offspring [22, 29] and one study found a statistically not significant trend towards higher rates of stillbirth or neonatal death [29]. In addition, pregnant women with a history of gastric bypass might be at risk to develop an internal hernia, potentially leading to severe consequences like bowel necrosis or acute perforation, which might eventually lead to acute C-Section [30]. Exceptional cases of maternal and fetal death have also been described [31, 32]. These aspects will be addressed and discussed in detail in the following paragraphs.

Reproductive aspects

Obesity was shown to impact fertility on various levels by affecting endometrial and ovarian function [33–35]. Insulin resistance and compensatory hyperinsulinemia adversely affect intraovarian follicle growth and oocyte maturation, leading to oligo-/amenorrhea, hyperandrogenemia and polycystic ovarian syndrome (PCOS) [36, 37]. Consequently, a close interaction of impaired reproductive and metabolic features can be observed in obese women [38]. Hence, even at a young age, assisted reproductive technology (ART) is often required in obese patients to achieve a live-birth. The accompanying technical procedures such as ovarian ultrasound visualization or oocyte retrieval might be complicated by excess body weight [35]. Even when ART can be performed, obesity was associated with impaired treatment outcome including less collected oocytes after ovarian hyperstimulation, lower embryo quality, reduced pregnancy and live-birth rates and high miscarriage rates. Although the available data is still inconclusive, it seems that those impaired ART outcomes are attributable to obesity and not to underlying pathologies such as PCOS [39]. Therefore, in accordance with the general BS guidelines [3] and depending on the individual patient's metabolic and reproductive profile, BS might be considered in infertile anovulatory patients with a BMI > 35 kg/m^2 and no effect of life-style intervention for at least 6 months [40]. Bariatric surgery was shown to ameliorate hyperandrogenemia and PCOS in a majority of patients [41]. In patients trying to conceive after BS, one meta-analysis reported up to 58% spontaneous conception rates [42]. Moreover, self-esteem and sexual functioning are increasing following BS induced weight-loss [43]. Even patients undergoing ART before and after BS showed increased numbers of retrieved oocytes, improved oocyte quality and live-birth rates [44]. However, risks and benefits of BS at childbearing age should be carefully balanced, in order to improve maternal health and to reduce the risk of long-lasting health consequences in the offspring [35]. BS should not be regarded as a primary infertility treatment [23].

Nutritional aspects

Deficiency Anemia

During pregnancy, hemoglobin (Hb) and hematocrit (Hct) levels decrease physiologically due to an expansion of blood volume by approximately 50% and red blood cell mass by only approximately 25% [45]. Pregnant women need to mobilize additional iron to meet the requirements of the growing fetoplacental unit, amounting to 1,200 mg during the course of pregnancy [46]. Although the absorption of iron is increased during pregnancy, it seems that an appropriate diet alone is not sufficient to meet those requirements, especially for women with a low pre-pregnancy iron status (Ferritin level < 30 g/L) [47]. Thus, iron-deficiency anemia (IDA) is the most frequent form of anemia in pregnant women. According to the WHO, anemia, defined as Hb levels of < 11 mg/dl in pregnant women, affects 41.8% of this population subgroup worldwide, with iron deficiency accounting for approximately 50% of cases [48].

There also seems to be a link between obesity and an altered iron metabolism. Obesity is considered to be a state of chronic inflammation, leading to increased levels of the acute-phase reactant hepcidin which inhibits the enterocyte iron absorption. Other factors such as inflammatory-induced sequestration of iron to the reticuloendothelial system and higher iron requirements due to larger blood volume add to the association between obesity and hypoferremia [49].

Weight loss after BS results in falling serum hepcidin levels and potentially improved iron status [50]. Patients who underwent malabsorptive surgery, however, showed an increase in anemia rates (anemia prevalence from 12.2% at baseline to 25.9% after 2 years, prevalence of low ferritin levels from 7.9% at baseline to 23.0% after 2 years) which can be attributed to a reduced caloric intake, intolerance for red meat, reduced acid production of the stomach and subsequently decreased bioavailability of dietary iron and the bypass of food through the duodenum [26]. A history of BS before pregnancy seems to increase the risk for the development of IDA during pregnancy [51, 52]. One study indicates that the rate of severe anemia might be higher in pregnancies that occur more than 4 years after RYGB surgery, leading to the conclusion that the time to conception might also be of importance [53]. However, all studies on the topic have limitations and further research is required to reinforce the currently available supplementation recommendations for the prevention of IDA in pregnant women after BS [22, 52, 54]. As IDA during pregnancy has adverse effects on pregnancy outcome (e.g. an increased risk for preterm delivery [55, 56]), prevention is however crucial. Also, maternal iron deficiency seems to have long term health effects on the offspring, mainly neurobehavioral abnormalities and an elevated cardiovascular disease risk [46, 57]. The ACOG recommends a daily intake of 27 mg of ferrous iron during pregnancy for patients without a history of BS [45], the WHO recommends 30 to 60 mg of elemental iron [58]. According to the current literature, the recommended supplementation dose for the prevention of IDA in non-pregnant women with a history of BS is 45 to 130 mg iron daily [59, 60], whereas the currently available recommendation for pregnant women after RYGB ranges from 40 to 600 mg of ferrous iron daily [24, 61, 62]. Any dose within this range should therefore be applicable; however, frequent laboratory tests should be performed and the dose adapted according to the results [61, 62]. The ACOG recommends a complete blood count and measurement of iron and ferritin every trimester [23].

Folic acid and Vitamin B12 deficiency can also lead to maternal anemia. The folic acid demand increases from 50 to 400 g per day during pregnancy and cannot always be met by diet alone, leading to folic acid deficiency being the most common cause for macrocytic anemia (MCV > 100 fL) during pregnancy [45]. Folic acid deficiency seems to be rare after all BS procedures [26, 63, 64]. The Endocrine Society Clinical Practice Guideline recommends biochemical monitoring preoperatively and 6, 12, 18 and 24 months after surgery and then in annual intervals only for patients after malabsorptive or combined procedures. A daily supplement of 400 g of folic acid should also be performed [59]. The American Association of Clinical Endocrinologists also recommends pre- and postoperative routine screening only for patients after malabsorptive or combined BS and also a daily supplement of 400 g of folic acid for all women of reproductive age [60]. Gascoin et al. compared non-obese pregnant controls with pregnant women after gastric bypass who took 800 g/day of folic acid and did not observe folic acid deficiency in the bariatric group [63]. Weng et al. could also find no evidence of folate deficiencies in patients after RYGB. They suggest that folate absorption occurs throughout the entire small intestine and any deficiency caused by inadequate dietary intake can therefore easily be corrected by supplementation [26]. Jans et al. report folate deficiency in 0 to 16% of pregnancies after BS with no adverse clinical outcomes [54]. As there is still controversy regarding the benefit of folic acid supplementation on pregnancy outcomes [65], it seems prudent to follow the general folic supplementation recommendations for pregnant women and screen for folate deficiency every trimester [60]; which is also supported by the ACOG [23].

Vitamin B12 deficiency anemia is mostly seen in women after gastric resection or with Crohn's disease [45]. The additional requirement of vitamin B12 during pregnancy is estimated to be 0.2 g/day [66]. Vitamin B12 deficiency seems to occur especially after malabsorptive or combined BS as the secretion of intrinsic factor and gastric acid is decreased and the duodenum, being the main absorption site, is bypassed. Incidence of Vitamin B12 deficiency after RYGB is reported to be between 4 and 62% [59, 67], with a tendency to increase over the course of time, possibly due to the fact that the body's reserves are able to cover the decreased absorption at early stages [26]. In pregnant women after BS, the prevalence of Vitamin B12 deficiency is reported to be between 48 and 53% [54], but not in bariatric gravidas who received a Vitamin B12 supplementation of 4 g/day and 1,000 g/month [63]. The Endocrine Society recommends biochemical monitoring preoperatively; 6, 12, 18 and 24 months after surgery and then in annual intervals only for patients after malabsorptive or combined procedures. With regards to the supplementation dose, recommendations for non-pregnant individuals range from 1,000 g intramuscularly (im) every 3 months to 1,000 g/week intranasally [59]. The American Association of Clinical Endocrinologists recommends pre-operative and annual screening for Vitamin B12 deficiency in patients after malabsorptive and combined bariatric procedures and a supplementation of 1,000 g/day orally or 500 g/week intranasally or 1,000 g/month parenterally [60]. For pregnant women after BS Kaska et al. recommend 350 g/day sublingually or 1,000 g/month im [61] and Busetto et al. recommend 350 to 500 g/day orally or 1,000 g/month im or 3,000 g every 6 months im or 500 g/week intranasally [24]. Although the available data is still conflicting, vitamin B12 deficiency seems to be associated with a higher risk of preterm birth [68], recurrent abortion, low birth weight (LBW), intrauterine growth retardation (IUGR), neural tube defects and impaired cognitive development [69]. Therefore, obstetricians should assess the Vitamin B12 status of pregnant women after BS every trimester and treat deficiencies accordingly [24, 60].

Vitamin D, calcium and bone metabolism

Several studies have examined the relationship between post-BS pregnancy, calcium and vitamin D metabolism and found a Vitamin D deficiency in 3% to over 70% of pregnant women, depending on the BS procedure [51, 54, 70]. There is a physiological increase in the need of vitamin D and calcitriol during pregnancy seemingly related to the calcium transfer to the fetus, particularly in the last trimester [70].

Vitamin D is converted from 7-dehydrocholesterol by the skin after exposure to sunlight or provided through diet (oily fish, mushrooms, fortified cereals, egg yolks and dietary supplements). The ingested or converted vitamin D has to be activated in order to exert its functions, like increasing intestinal calcium uptake and promoting calcium and phosphate mobilization from the bone [71, 72]. The altered anatomy of the intestinal tract occurring especially after RYGB could directly interfere with calcium absorption, possibly leading to maternal bone loss, reduced calcium levels in breast milk or deficient fetal bone mineralization [61]. A possible association between vitamin D insufficiency during pregnancy and SGA offspring, perhaps by the impediment of intestinal calcium absorption or increase of inflammatory cytokines and cellular oxidative stress, is currently discussed [73–75].

Additionally, low vitamin D levels are often associated with higher levels of parathormone, causing secondary hyperparathyroidism and increasing the risk of accelerated bone remodeling, leading potentially, among other factors, to a lower bone mineral density in bariatric patients compared to non-surgical controls [76].

Inadequate Vitamin D levels (< 29 ng/ml) were observed in over 70% of pregnant women who underwent RYGB surgery, through all three trimesters of pregnancy and despite a supplementation with 600 IU of Vitamin D per day. The prevalence of elevated PTH levels (> 65 pg/ml) was highest in the third trimester with 32.6% of subjects. However, no adverse pregnancy outcomes were detected [70]. A large retrospective study conducted in Taiwan pointed out that there is a high incidence of post-surgery secondary hyperparathyroidism for all procedures (37.2%) which could lead to a higher long-term fracture risk, however, the available data ins still controversial. Long term follow up of the bone's health in patients with a history of BS should however be considered [77]. Nutritional assessment, periodical blood examinations and aimed vitamin D supplementation are pivotal in maintaining physiological levels of vitamin D, calcium and PTH [24, 73, 74, 78]. The current US daily consumption recommendation for vitamin D is 600 IU and the toxicity limit is estimated to be between 10,000 and 40,000 IU/day [79]. The supplement dosage recommendations for post bariatric pregnant women range from 1,000 IU / day to 6,000 IU / day, with 1,000 to 2,000 mg of calcium citrate per day [24, 61]. Pregnant women should be screened for Vitamin D inadequacy at least once every trimester [23].

Protein deficiency

BS might be associated with protein deficiency as a consequence of the restricted food intake and absorption. Protein deficiency should be suspected in case of fatigue, weakness and hair loss. [80]. It can be diagnosed through clinical examination including muscle mass tests or, in case of severe protein deficiency, low serum albumin values [27, 80]. Patients occasionally develop edema and in rare cases anasarca [81, 82].

A German study in non-pregnant patients after BS provided evidence that 60 g/daily or even higher levels of protein supplements increase body fat mass loss without negative effects on the renal function [83].

The recommended protein intake for pregnant women after BS is 60 g daily [24] and the ACOG guidelines support this recommendation [23]. There is only little evidence for detrimental effects of maternal protein deficiency on pregnancy outcome, mainly impaired fetal growth [84]; however, pregnant women after BS should be advised to adhere to the general recommendations for post-surgery protein intake and the fetal growth should be assessed regularly [23, 24].

Other nutrients

The American Guidelines for the perioperative support of BS patients recommend routine screening for vitamin deficiencies, in order to prevent long term complications. For pregnant women, a screening every trimester is recommended [60].

Vitamin A deficiency was reported in 10% to 58% of pregnant women after BS, depending on BS procedure and gestational age [51, 61, 85].Vitamin A, alone or in combination with other fat-soluble vitamins (D, E, K), has to be supplied if deficiencies are present [60, 61]. Next to being an important antioxidant in the body, Vitamin A is also involved in cell signaling pathways. There is some evidence that antenatal Vitamin A supplementation reduces the risk of maternal anemia and the risk of maternal night blindness. Furthermore there is only weak evidence that antenatal vitamin A supplementation could reduce the risk of maternal infection [86]. The vitamin A supplement dose should not exceed 5,000 IU/day due to its teratogenic effects and should be administered in the form of beta-carotene [24, 61, 87].

Gascoin et al. observed also vitamin E deficiency in pregnant women with a history of gastric bypass, but no adverse pregnancy outcome are described [63].

Next to selenium, which plays an important role in several enzymatic reactions in the body, deficiencies of Vitamins C, B1 and B9 in pregnant women after BS were observed. Moreover, the offspring of mothers with a BS history displayed lower cord blood levels of several micronutrients such as Vitamin A, calcium, zinc and iron, in contrast to a control group [63].

Because of the limited number of participants in the available studies, no practical guidelines containing thresholds or dosage recommendations for the treatment of micronutrients deficiencies in post-surgical pregnancies have been created so far [51], however, all available statement papers recommend the supplementation of vitamins in pregnant women after BS [23, 24, 35, 61].

Glucose metabolism and gestational diabetes

Gestational Diabetes Mellitus (GDM) is defined as "diabetes first diagnosed in the second or third trimester of pregnancy that is not clearly either preexisting type 1 or type 2 diabetes" [88] and affects approximately 6% of pregnancies in Europe [89]. Most recent guidelines recommend universal testing for GDM between 24 + 0 and 28 + 6 weeks of gestation by a 2 h 75 g oral glucose tolerance test (OGTT) [88]. The International Association of Diabetes in Pregnancy Study Group (IADPSG) established the following diagnostic thresholds: fasting plasma glucose ≥5.1 mmol/l (92 mg/dl), or 1-h plasma glucose ≥10.0 mmol/l (180 mg/dl), or 2-h plasma glucose ≥8.5 mmol/l (153 mg/dl) [90]. However, the diagnosis of GDM still remains controversial, as other diagnostic algorithms and thresholds are still in use [91], leading to heterogeneity in study results and epidemiologic data [89].

Obesity is a risk factor for the development of GDM. Compared to normal weight women, the OR for GDM was found to be 1.97 in overweight women (pre-pregnancy BMI 25 to 30), 3.01 in moderately obese (BMI 30 to 35) and 5.55 in severely obese women (BMI > 35) [92]. The mechanisms which link obesity and GDM are still a target of research, but the enhanced secretion of pro-inflammatory cytokines by adipose tissue and subsequent systemic inflammatory and immune dysregulation seems to increase the maternal insulin resistance [93, 94].

GDM is associated with a number of adverse pregnancy outcomes, especially cesarean section, large for gestational age, macrosomia and preeclampsia [91, 95]. Moreover, children of diabetic mothers seem to have an increased risk of developing obesity and metabolic dysfunction later in life [8, 96, 97] due to "metabolic imprinting", e.g. the in-utero alteration of fetal organ function as a consequence of an excessive supply of nutrients and subsequently enhanced exposure to growth factors [96, 97].

BS before pregnancy seems to reduce the risk for developing GDM considerately [22, 52, 98–102]. Galazis et al. found the overall incidence of GDM as being approximately half in women after BS compared to controls [52]. However, results vary depending on control group and diagnostic criteria (see Table 1).

Despite the protective effect of BS and subsequent weight loss on the development of GDM, some procedures like RYGB alter glucose kinetics and might also have detrimental effects on pregnancy outcome and GDM diagnostics which have to be observed by obstetricians.

As previously observed in non-pregnant patients, some bariatric procedures (like RYGB and sleeve gastrectomy) are characterized by an exaggerated postprandial rise of plasma glucose concentrations followed by hyperinsulinemic hypoglycemia [103]. To provide first insights into the possible effects of gastric bypass surgery on glucose metabolism during pregnancy, we retrospectively assessed maternal characteristics of 76 pregnant women after gastric bypass. The data included results of a 2 h 75 g OGTT with measurements at fasting as well after 60 and 120 min after oral glucose load. We found that women after gastric bypass had improved fasting glucose, but altered patterns of postprandial glucose dynamics including a rise at 60 min, followed by hypoglycemia at 120 min in more than half of pregnant patients [28]. Our results were recently confirmed by another prospective cohort study on 25 pregnant women after RYGB, indicating that the recommended diagnosis criteria for GDM are not reliable after BS [104]. Obstetricians should consider other diagnostic approaches such as frequent capillary blood glucose measurements or continuous subcutaneous glucose monitoring (CGMS) in these patients; however, there are no guidelines yet [23, 24, 35, 105]. Only one study reported CGMS profiles of 35 pregnant women after RYGB and reported abnormal glucose variability in real-life conditions as well [106]. Therefore, obstetricians should be aware of symptoms indicative of dumping syndrome. The early dumping syndrome occurs within 15 min to 1 h after a meal rich in simple carbohydrates. The rapid emptying of hyperosmolar carbohydrates into the small intestine leads to a fluid shift from plasma to bowel, causing a drop in blood pressure and subsequent compensation, leading to

Table 1 Results of meta-analysis of studies comparing the risk for the development of GDM in women after BS with different subgroups, adapted from Galazis et al. [52]

Control Group	No. of Studies	Participants		OR (95% CI)	*p*-Value
		BS	Control		
Overall	15	2724	136,075	0.47 (0.40–0.56)	< 0.001
Women after BS vs. obese controls	6	1292	133,777	0.34 (0.18–0.67)	< 0.001
Women after BS vs. same women before BS	5	377	343	0.71 (0.45–1.11)	0.14
Women after BS vs. other women before BS	3	1171	916	0.42 (0.22–0,79)	0.007
Women after BS vs. pre-pregnancy BMI matched obese women without BS	3	433	1537	0.77 (0.22–2.65)	0.68
Women after BS vs. pre-surgery BMI matched obese women without BS	6	864	133,388	0.24 (0.10–0.54)	< 0.001

vasomotor symptoms such as flushing, palpitation, perspiration, tachycardia, hypotension and syncope [107, 108]. Patients should be advised to consume smaller meals rich in complex carbohydrates, to delay liquid intake until at least 30 min after a meal and to lie down after eating to delay the gastric emptying into the small intestine [108]. The late dumping syndrome, with an onset of symptoms 2 to 3 h after a meal, is supposed to be caused by an excessive insulin response following the rapid glucose transit into the jejunum and subsequent reactive hypoglycemia [107, 108]. The symptoms include sweating, tremulousness, poor concentration, altered consciousness, palpitations and syncope. The main therapeutic intervention is a dietary modification eliminating refined carbohydrates. Pectin or guar gum can be added to increase viscosity of food but are poorly accepted due to their unpalatability. Diaxozide decreases the insulin release and has been reported to ameliorate the condition but is not safe in pregnancy; somatostatin analogues and acarbose are not well tested in pregnant human individuals and there is only one case report on successful treatment of late dumping syndrome with acarbose in a pregnant woman [107]. Obstetricians should seek advice from bariatric specialists if their pregnant patients present with symptoms indicative of dumping syndrome.

Preeclampsia and hypertensive disorders

Hypertensive disorders in pregnancy include pre-gestational chronic hypertension, pregnancy-induced hypertension (PIH) and preeclampsia (PE). PE is defined as de novo onset of hypertension (> 140 mmHg systolic or > 90 mmHg diastolic) after 20 weeks gestation and the coexistence of at least one of the following conditions: proteinuria, other maternal organ dysfunction such as renal insufficiency, liver involvement or neurological complications or utero-placental dysfunction (fetal growth retardation) [109]. Hypertensive disorders affect approximately 10% [110] of all pregnancies and account for 14% of maternal deaths worldwide [111]. Its incidence is on the rise, with a 21% increase in inpatient deliveries involving PE between 2005 and 2014 in the USA [112]. Several authors attribute the increasing PE incidence to the obesity pandemic [113–115]. Mbah et al. report a positive association between PE incidence and pre-pregnancy BMI as well as pregnancy weight gain rate, with 3.3% of normal weight mothers being affected, 7.7% of mothers with class I obesity, 9.5% of mothers with class II obesity, 10.9% of mothers with class III obesity and 13.4% of super obese gravidas (BMI ≥ 50 kg/m^2). In comparison to normal weight mothers, obese women had a three-fold increased risk for the development of PE [113]. Although the mechanisms by which obesity increases the risk for hypertensive disorders are not fully understood yet, it seems that obesity-related metabolic factors cause cytotrophoblast dysfunction and subsequent placental ischemia, thereby increasing the release of soluble placental factors and enhancing the sensitivity by which those factors cause endothelial dysfunction and hypertension [115]. With BS being the most effective treatment for obesity, it can be assumed that women who conceive after BS have a lower risk for developing hypertension disorders and the available data support this presumption. One study compared women who delivered before an already planned BS with women who delivered after BS. Almost 15% of women who delivered before BS had PE compared to only 3% of those who delivered after BS. Rates of PIH were also lower in the post-surgery group (2.5% versus 13.0%), resulting in a 75% lower odds to be diagnosed with a hypertensive disorder for women after surgery [116]. Several reviews and meta-analysis [22, 98–102, 117] come to the same conclusion. Yi et al. [102] report an overall OR of 0.42 for the diagnosis of hypertensive disorders in pregnancies after BS, with a significantly less OR (0.14) when conception took place within the first 2 years after surgery. Vrebosch et al. [99] come to the conclusion that the incidence of PE and PIH are lower in post-surgical women compared to obese non-surgical controls, but still higher than in normal weight women without BS, but only reviewed laparoscopic adjustable gastric banding studies. Ducarme et al. [118] found evidence that PE rates were lower in women after BS, but not different for PIH. Although the available data indicates that gravidas after BS are at significantly lower risk for the diagnosis of hypertension disorders, further research is needed, especially concerning the impact of different surgical procedures and surgery-conception time.

Surgical complications

Pregnancy may expose women after BS to a higher risk of developing internal herniation due to the fact that the enlarged uterus lifts up the bowel, resulting in increased intra-abdominal pressure [24, 30]. In the case of acute abdominal pain, immediate surgical intervention must be considered, also when pregnancy has to be carried on [24, 30, 31, 119]. Of note, internal hernia after RYGB is not rare, with an incidence of up to 10% [30]. The most common internal hernias develop in the the transverse mesocolon defect, the Petersen's space and the mesenteric defect underneath jejunu-jejunalis anastomosis [120]. Petersen's hernia is a retroanastomotic hernia where the small bowel moves into the space between the caudal surface of the transverse mesocolon and the edge of the Roux limb and can rapidly lead to acute bowel obstruction with necrosis. In this case an immediate emergency surgery has to be performed [121]. Patients who are suspected to have developed an internal hernia are requested to fast during observation. If the abdominal pain relapses after the ingestion of food a subacute operation has to be considered. If the pain is constantly present in spite of fasting, an emergency operation (detorsion or bowel resection) is necessary and should be performed as fast as possible to minimize the risk of bowel necrosis and severe maternal and fetal complications [122].

Fetal malformations

Obesity during pregnancy might be associated with a higher risk of fetal malformations like neurological defects, congenital heart defects and orofacial clefts. Furthermore, some data indicate that the risk of miscarriage and intrauterine fetal death could be increased [4]. A systematic review and meta-analysis assessed the risk of congenital anomalies in the offspring of obese pregnant women compared to lean pregnant women and found that neonates of obese women have a higher risk of neural tube defects (anencephaly OR: 1.39, CI: 1.03–1.87, spina bifida OR: 2.24, CI: 1.86–2.69), cardiovascular defects (OR: 1.30, CI: 1.12–1.51), and other congenital abnormalities such as anorectal atresia (OR 1.48, CI: 1.12–1.97), compared to pregnant women with normal BMI [7]. More recent studies come to similar conclusions [123].To date, the role of obesity in inducing fetal malformations is not fully understood and may reflect the difficulty of prenatal diagnosis at early pregnancy, due to obesity-related procedural difficulties. Further research is needed to elucidate the relationship between obesity and fetal malformations [123, 124].

Fetal and neonatal complications

It is widely known that maternal obesity could lead to LGA offspring, which poses a high risk for complications during labour, like shoulder dystocia [125], and also to long-term health consequences, like obesity in childhood, diabetes and cardiovascular diseases [126]. Thus, it is reasonable to investigate if BS and consequent weight lost could also influence the children of mothers with a history of BS.

A Swedish national cohort study investigated the outcomes of 670 singleton pregnancies of post-surgical women and detected that pregnant women who underwent BS have a lower risk of gestational diabetes and large for gestational age (LGA) neonates, but a higher risk of SGA infants. No significant difference in the frequency of fetal malformations was found [29].

Several other studies (Table 2) found an increased risk of SGA infants born to mothers after malabsorptive or mixed bariatric surgeries [22, 52, 100, 102, 117], but not after solely restrictive procedures [52, 99]. The pathophysiology of this phenomenon requires further elucidation, but there seems to be an association between low maternal glucose levels in glucose challenge or oral glucose tolerance tests and SGA fetuses [95, 127]. An association between lower neonatal weight, glucose nadir and increased insulin release during an OGTT was most recently observed by our study group in offspring of mothers after RYGB [104]. In addition, Gascoin et al. found a significant inverse correlation between birth weight and length and maternal weight loss between surgery and pregnancy (the greater the weight loss the lower the birth weight and length). There were also low cord blood IGF1 and Leptin levels in infants from RYGB mothers, hinting to a decreased anabolism in those infants [63]. Low birth weight seems to have detrimental effects on the offspring even in adulthood. Being born SGA is considered to be a risk factor for the development of insulin resistance and type 2 diabetes, the metabolic syndrome and cardiovascular diseases [128], possibly due to fetal programming by changes in the intrauterine environment in malnourished mothers (thrifty phenotype hypothesis) [129]. Therefore, it might even be considered to prefer restrictive over malabsorptive BS techniques in young women who have a desire to bear children to avoid those complications [52].

However, two retrospective studies conducted in Israel and in France compared fetal birth weight after malabsorptive and restrictive procedures and found no statistically significant difference in SGA rates between the two groups [130, 131].

Table 2 Overview on the SGA risk after bariatric surgery, comparing malabsorptive to restrictive surgery, adapted from Johansson [29] Gascoin [63] Chevrot [139] Sheiner [101] and Ducarme [118]

Control Group	Study	Participants	SGA	SGA after malabsorptive surgery	SGA after restrictive surgery	*p*-Value
Women after BS vs obese controls	Johansson	670/2356	15.6% vs 7.6%	n.d.	n.d.	< 0.001
Women after BS vs lean pregnant women	Gascoin	56/56		n.d	n.d.	NS
Women after malabsorptive surgery vs women with restrictive surgery	Chevrot	58/81	n.d.	17	7	< 0.001
Women after restrictive vs women after malabsorptive surgery	Sheiner	394/55	n.d.	7.3	12.8	NS
Women after RYGB vs women after LAGB	Ducarme	31/63	n.d.	32.3%	17.1%	NS

Breastfeeding

Human breast milk is a rich source of carbohydrates, protein, fat, vitamins, minerals, digestive enzymes and hormones (87% water, 3.8% fat, 1.0% protein, and 7% lactose). Additionally, it contains a vast amount of other, at least partially bioactive compounds, such as immune cells and human milk oligosaccharides (HMOs). These HMOs were found to exert antibacterial effects in the infant's gastrointestinal tract. Regarding micro-nutrition, human milk supplies sufficient amounts of all vitamins except Vitamin D and vitamin K. Therefore, the lack of these two vitamins carries out some risk of deficiency for the infant [132].

Vitamin B12 deficiency might be a problem in breastfed infants born to women after gastric bypass, potentially leading to detrimental consequences such as polycythemia or megaloblastic anemia [133]. As observed in one case the milk secreted by lactating women after gastric bypass could be of lower nutritional density, especially in milk fats. This could lead to delayed growth of the children when breastfed exclusively as it was observed in one case report [134]. However, breastfeeding is known to prevent several infectious, atopic and cardiovascular diseases. Breastfeeding may also reduce the risk of respiratory infections, asthma, leukaemia and sudden infant death syndrome [135]. It also provides positive effects on brain and neuronal development and might be associated with a higher IQ [136]. Other studies concluded that exclusive breastfeeding for longer than six months may reduce the risk of obesity in later life [137]. As there is very little evidence regarding nutrient deficiencies in breast milk after BS, it is reasonable to recommend bariatric patients to breastfeed their infants [24, 138]. The above-mentioned positive effects of human breast milk most likely outweigh any BS related deficiency. However, there is no international consensus regarding vitamin or micronutrient supplementation during the lactational period after BS and healthcare professionals should take the patients history of BS into consideration when their infants present with symptoms of any nutritional deficiency.

Limitations

The limitations of this study result from its narrative approach. Compared to systematic reviews or meta-analysis, narrative reviews are characterized by subjective study selection and weighing. Inclusion criteria and study characteristics are mostly unspecified which may cause misleading in drawing conclusions. To be able to elaborate objective guidelines for the management of pregnancies after BS, systematic reviews and meta-analysis should be performed.

Conclusion

History of BS is associated with several risks for the mother and the fetus. Women who want to conceive should have a preconception counseling to be informed about the risks of pregnancy after BS, like malnutrition, deficiency and subsequent supplement of micronutrients, internal hernia and SGA infants. Regular blood examinations and regularly performed ultrasounds of the growing fetus (growing-curve, umbilical Doppler, amniotic fluid index) are necessary. Furthermore, the OGTT should not be performed as a routine test for the screening of gestational diabetes, because of the high risk of hypoglycemia. Ideally, pregnant women should be taken care of by a specialized center offering a multidisciplinary team with experience in the management of pregnancies after BS.

Any severe upper abdominal pain must be taken seriously because of the high risk of internal hernia. Of note, an international treatment consensus for pregnancy after BS is missing due to its novelty; hence specific recommendations of way of delivery or breastfeeding are not yet available. However, within the next years the number of pregnant BS patients and possible complications will increasingly challenge obstetricians.

Abbreviations

ACOG: American Congress of Obstetricians and Gynaecologists; ART: Assisted Reproductive Technology; BE: Bariatric endoscopy; BMI: Body Mass Index; BS: Bariatric surgery; CGMS: Continuous subcutaneous glucose monitoring; C-section: Cesarean section; GDM: Gestational diabetes mellitus; Hb: Hemoglobin; Hct: Hematocrit; HMO: Human milk oligosaccharides; IADPSG: International Association of Diabetes in Pregnancy Study Groups; IDA: Iron deficiency anemia; IGF1: Insulin-like growth factor 1; im: intramuscular; IQ: Intelligence quotient; IU: International Units; IUGR: Intrauterine growth retardation; LAGB: Laparoscopic gastric banding; LBW: Low birth weight; LGA: Large for gestational age; MCV: Mean Corpuscular Volume; OGTT: Oral glucose tolerance test; OR: Odds ratio; PCOS: Polycystic Ovary Syndrome; PE: Preeclampsia; PIH: Pregnancy-induced hypertension; PTH: Parathyroid hormone; RYGB: Roux-en-Y gastric bypass; SGA: Small for gestational age; WHO: World Health Organization

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Availability of data and materials

The data supporting the conclusions of this article is included within the article.

Authors' contributions

VF contributed to the acquisition, preparation and interpretation of the data and was the main contributor in writing the manuscript. TS contributed equally to the acquisition, preparation and interpretation of the data and was the second main contributor in writing the manuscript. MF contributed to the discussion of obstetric implications and fertility related issues and the general drafting of the manuscript. WE contributed to the discussion of obstetric implications, general therapeutic recommendations and drafting of the manuscript. GP contributed to acquisition of data and the discussion of surgical implications. PH contributed to the discussion of obstetric implications, to the interpretation of the data and drafting of the manuscript. CG contributed to the acquisition, preparation and interpretation of the data, the discussion of obstetric implications and the drafting of the manuscript. All authors reviewed and approved the final manuscript.

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RESEARCH ARTICLE

Pregnancy after bariatric surgery and adverse perinatal outcomes: A systematic review and meta-analysis

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Abstract

Background

Women who undergo bariatric surgery prior to pregnancy are less likely to experience comorbidities associated with obesity such as gestational diabetes and hypertension. However, bariatric surgery, particularly malabsorptive procedures, can make patients susceptible to deficiencies in nutrients that are essential for healthy fetal development. The objective of this systematic review and meta-analysis is to investigate the association between pregnancy after bariatric surgery and adverse perinatal outcomes.

Methods and findings

Searches were conducted in Medline, Embase, PsycINFO, CINAHL, Scopus, and Google Scholar from inception to June 2019, supplemented by hand-searching reference lists, citations, and journals. Observational studies comparing perinatal outcomes post-bariatric surgery to pregnancies without prior bariatric surgery were included. Outcomes of interest were perinatal mortality, congenital anomalies, preterm birth, postterm birth, small and large for gestational age (SGA/LGA), and neonatal intensive care unit (NICU) admission. Pooled effect sizes were calculated using random-effects meta-analysis. Where data were available, results were subgrouped by type of bariatric surgery. We included 33 studies with 14,880 pregnancies post-bariatric surgery and 3,979,978 controls. Odds ratios (ORs) were increased after bariatric surgery (all types combined) for perinatal mortality (1.38, 95% confidence interval [CI] 1.03–1.85, $p = 0.031$), congenital anomalies (1.29, 95% CI 1.04–1.59, $p = 0.019$), preterm birth (1.57, 95% CI 1.38–1.79, $p < 0.001$), and NICU admission (1.41, 95% CI 1.25–1.59, $p < 0.001$). Postterm birth decreased after bariatric surgery (OR 0.46, 95% CI 0.35–0.60, $p < 0.001$). ORs for SGA increased (2.72, 95% CI 2.32–3.20, $p < 0.001$) and LGA decreased (0.24, 95% CI 0.14–0.41, $p < 0.001$) after gastric bypass but not after gastric banding. Babies born after bariatric surgery (all types combined) weighed over 200 g less than those born to mothers without prior bariatric surgery (weighted mean difference

Abbreviations: BMI, body mass index; BPD, biliopancreatic diversion; CI, confidence interval; GWG, gestational weight gain; IPD, individual patient data; LAGB, laparoscopic adjustable gastric banding; LGA, large for gestational age; NICU, neonatal intensive care unit; NR, not reported; OR, odds ratio; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; SGA, small for gestational age; WMD, weighted mean difference.

−242.42 g, 95% CI −307.43 to −177.40 g, $p < 0.001$). There was low heterogeneity for all outcomes ($I^2 < 40\%$) except LGA. Limitations of our study are that as a meta-analysis of existing studies, the results are limited by the quality of the included studies and available data, unmeasured confounders, and the small number of studies for some outcomes.

Conclusions

In our systematic review of observational studies, we found that bariatric surgery, especially gastric bypass, prior to pregnancy was associated with increased risk of some adverse perinatal outcomes. This suggests that women who have undergone bariatric surgery may benefit from specific preconception and pregnancy nutritional support and increased monitoring of fetal growth and development. Future studies should explore whether restrictive surgery results in better perinatal outcomes, compared to malabsorptive surgery, without compromising maternal outcomes. If so, these may be the preferred surgery for women of reproductive age.

Trial registration

PROSPERO CRD42017051537.

Author summary

Why was this study done?

- Obesity during pregnancy increases the risk of health complications for both mother and baby.
- Bariatric surgery before pregnancy improves obesity-related problems for the mother but reduces the absorption of micronutrients that are needed for healthy fetal development.
- This research aimed to investigate whether bariatric surgery is associated with adverse outcomes for the baby.

What did the researchers do and find?

- This systematic review included 33 studies that investigated perinatal outcomes among women with previous bariatric surgery compared to women without previous bariatric surgery.
- Meta-analysis identified a significant increase in odds of perinatal mortality, congenital anomalies, preterm birth, and neonatal intensive care unit admission but a decrease in odds of postterm birth after bariatric surgery.
- The odds of small babies were increased and the odds of large babies were decreased after malabsorptive bariatric surgery types, but there was no change for restrictive bariatric surgery types.

What do these findings mean?

- Bariatric surgery, in particular malabsorptive types of surgery, seems associated with an increased risk of some adverse perinatal outcomes, which suggests a link with nutrition.
- Women of reproductive age undergoing bariatric surgery are a high-risk group and require specialised preconception and antenatal nutritional support to achieve the best outcomes for both mothers and babies.

Introduction

Obesity is a global public health challenge with over 650 million adults affected worldwide, and prevalence continues to rise, making obesity the most common medical condition in women of reproductive age [1,2]. Maternal obesity, defined as prepregnancy body mass index (BMI) $\geq$ 30 kg/m^2, has severe implications for both mother and baby. Maternal risks include higher likelihood of gestational diabetes, preeclampsia, and cesarean section [3]. For the neonate, there is increased risk of pre- and postterm birth, small and large for gestational (SGA/LGA), congenital anomalies, and perinatal mortality [3,4]. Interventions to reduce maternal obesity are important not only to improve pregnancy outcomes but also to reduce the long-term health burden on the mother and offspring, including cardiovascular disease and insulin resistance [5].

Bariatric surgery is the most effective treatment for long-term weight loss, and over half of surgeries are performed on women of reproductive age [6,7]. Women who undergo bariatric surgery prior to pregnancy are less likely to experience comorbidities associated with obesity, such as gestational diabetes and hypertension [8]. However, micronutrient deficiencies are increased after bariatric surgery and may therefore have implications for fetal environment [9]. Maternal deficiencies in folate, iron, and vitamin D, for example, are all linked with adverse perinatal outcomes including neural tube defects, preterm birth, and low birth weight [10]. Malabsorptive procedures such as Roux-en-Y gastric bypass (RYGB) and biliopancreatic diversion (BPD) reduce the absorption of micronutrients because part of the small intestine is bypassed, whereas restrictive procedures such as laparoscopic adjustable gastric banding (LAGB) and sleeve gastrectomy (SG) reduce stomach capacity [11]. There have been multiple case reports of congenital anomalies occurring after malabsorptive procedures because of maternal malnutrition; however, the evidence from observational studies is conflicting [12].

Previous meta-analyses on pregnancy after bariatric surgery have focused on maternal outcomes, and there is limited evidence on perinatal outcomes other than size for gestational age and preterm birth [8,13,14]. The aim of this systematic review and meta-analysis was to compare adverse perinatal outcomes among women who underwent bariatric surgery prior to pregnancy with those who had not. When possible, the difference in effect size between malabsorptive and restrictive procedures was explored.

Methods

Search strategy and selection criteria

Searches were conducted in Medline, Embase, PsycINFO, CINAHL, Scopus, Google Scholar, and relevant e-journals from inception to June 3, 2019. We included observational studies published in the English language, involving women who had undergone bariatric surgery prior to pregnancy, and compared them to women without a history of bariatric surgery. We included studies that combined all types of bariatric surgery or provided data for RYGB, LAGB, SG, or BPD separately. The following perinatal outcomes were included: perinatal mortality (including stillbirth), congenital anomalies, preterm birth, postterm birth, SGA, LGA, neonatal intensive care unit (NICU) admission, birth weight, and gestational age.

The search strategy (S1 Table) included a mixture of keywords and MeSH headings: (pregnan* or mother* or matern*) and (bariatric surgery or weight loss and surgery or gastric bypass or gastric band* or sleeve or biliopancreatic diversion or LAGB or RYGB) and (death or mortality or newborn* or fetal or congenital or stillbirth or defect* or perinatal or obstetric or neonat* or outcome* or birth). Reference lists and citations were searched for all included primary studies and for relevant reviews identified by the database searches. Authors were contacted if additional data were required for inclusion in meta-analysis. Screening, data extraction, and quality assessment were carried out in duplicate.

This review was conducted in line with the PRISMA and MOOSE guidelines (S1 PRISMA Checklist) [15,16]. The protocol is published on PROSPERO (CRD42017051537).

Data analysis

The Cochrane Cohort Study data extraction tool was adapted to meet the requirements of this review. Study characteristics extracted included study design, study location, type of bariatric surgery, and control group. Frequencies, effect sizes, and confidence intervals (CIs) of adverse perinatal outcomes were also extracted. For continuous outcomes, means and standard deviations were extracted. When multiple studies reported data from the same cohort with the same participant inclusion criteria, the decision was made to include the study with the larger sample size for the exposed group. Studies with duplicate data were only included if they reported different perinatal outcomes and were therefore included in separate meta-analysis. The Newcastle-Ottawa quality assessment scale was used to appraise the quality of the included studies out of a maximum of eight points (S1 Fig). The studies were assessed for representativeness of the exposed cohort, selection of the nonexposed cohort, ascertainment of exposure and outcome, study design and analysis, and adequacy of follow-up.

A meta-analysis was used to calculate a pooled odds ratio (OR) and 95% CI when there were at least three studies reporting the same outcome. For continuous perinatal outcomes, a weighted mean difference (WMD) and 95% CI were calculated. DerSimonian and Laird random-effects model was used to take clinical heterogeneity into account such as unreported differences between surgical procedures (e.g., technique and limb length) and different levels of patient postsurgery and preconception care. When a study reported data on multiple control groups, a hierarchy was developed to firstly include the most comparable BMI group to the postbariatric patient, which was prepregnancy BMI matched, then obesity. When there was evidence of moderate heterogeneity ($I^2 > 40\%$), subgroup analysis by type of surgery or comparison group, as defined a priori, was carried out if three or more studies existed for each group. Any remaining heterogeneity was explored through meta-regression for factors including location, sample size, publication date, and quality. Publication bias was investigated using Egger's test and funnel plots. For studies reporting adjusted results, their crude and adjusted

ORs were compared to determine whether adjustments affected the effect size. Sensitivity analysis was performed for each meta-analysis by excluding one study at a time to identify the effect of any individual study on the pooled effect size and between-study heterogeneity. All analyses were conducted in Stata/SE 15.0.

Results

Study characteristics

Database searches identified 3,470 results for title and abstract screening, of which 141 studies underwent full-text assessment (Fig 1). The kappa statistic for inter-rater agreement of study inclusion between authors was 0.84 (scores > 0.81 are considered excellent) [17]. Thirty-seven studies met the inclusion criteria, but four were excluded because they reported the same cohort, participant inclusion criteria, and outcomes as another study [18–21]. This resulted in 33 studies that reported original data on perinatal outcomes (14,880 pregnancies after bariatric surgery and 3,979,978 pregnancies without bariatric surgery, Table 1). Fifteen of the included studies were conducted in Europe, 10 were conducted in the United States, three in Israel, two in each Australia and Brazil, and one in Canada. Studies were published between 1998 and 2018. All studies scored over five out of eight for quality, with 20 studies scoring at least seven (S2 Table). Many studies conducted more than one analysis with multiple surgery types or control groups. Sixteen analyses combined all bariatric surgery patients, whereas 14 studies were restricted to RYGB, six analyses included only LAGB, one included only SG, and one included BPD. Nine analyses compared women's postsurgical pregnancies to pre/early-pregnancy BMI–matched controls, and 14 used obesity controls (which were $\geq$30 kg/m^2, 35 kg/m^2, or 40 kg/m^2) in line with their relevant bariatric surgery guidelines, or matched for presurgical BMI. Eleven analyses compared pregnancies before and after bariatric surgery, nine compared outcomes to the general population, and five used healthy BMI as the control group.

Perinatal mortality and congenital anomalies

Perinatal mortality or stillbirth was reported in 10 studies. The pooled odds were significantly increased post-bariatric surgery compared to women without prior bariatric surgery (OR 1.38, 95% CI 1.03–1.85, $p = 0.031$) (Fig 2A) [22,25,26,34,39,41–43,45,52]. Ten studies reported on congenital anomalies, which were also found to have significantly increased odds post-bariatric surgery (OR 1.29, 95% CI 1.04–1.59, $p = 0.019$) (Fig 2B) [22,25,34,35,41,42,44,46,51,52]. There was no significant heterogeneity for either outcome ($I^2 = 12.1\%$, 95% CI 0.0–53.1, $p = 0.331$ and $I^2 = 28\%$, 95% CI 0.0–65.5, $p = 0.186$, respectively).

Gestational age

Preterm birth was reported in 20 studies, with 19 eligible for meta-analysis [22,27–30,32,34,36–39,42,44–47,49,51,53]. The overall odds of preterm birth were significantly increased post-bariatric surgery compared to women without prior bariatric surgery (OR 1.35, 95% CI 1.14–1.60, $p = 0.001$) (S2 Fig). There was significant heterogeneity ($I^2 = 50.1\%$, 95% CI 15.3–70.6, $p = 0.007$), which remained significant after subgroup analyses by control group but was reduced after subgrouping by type of surgery (Fig 3A). There were significantly increased odds of preterm birth after bariatric surgery in the 'all bariatric surgery' group (OR 1.57, 95% CI 1.38–1.79, $p < 0.001$). The association was not significant for subgroups 'RYGB' (OR 1.14, 95% CI 0.89–1.46, $p = 0.289$) or 'LAGB or SG' (OR 0.88, 95% CI 0.58–1.34, $p = 0.565$). The study excluded from the meta-analysis because of lack of crude data reported an adjusted OR for preterm birth of 1.43 (95% CI 1.01–2.03) post-bariatric surgery ($n = 293$) compared to

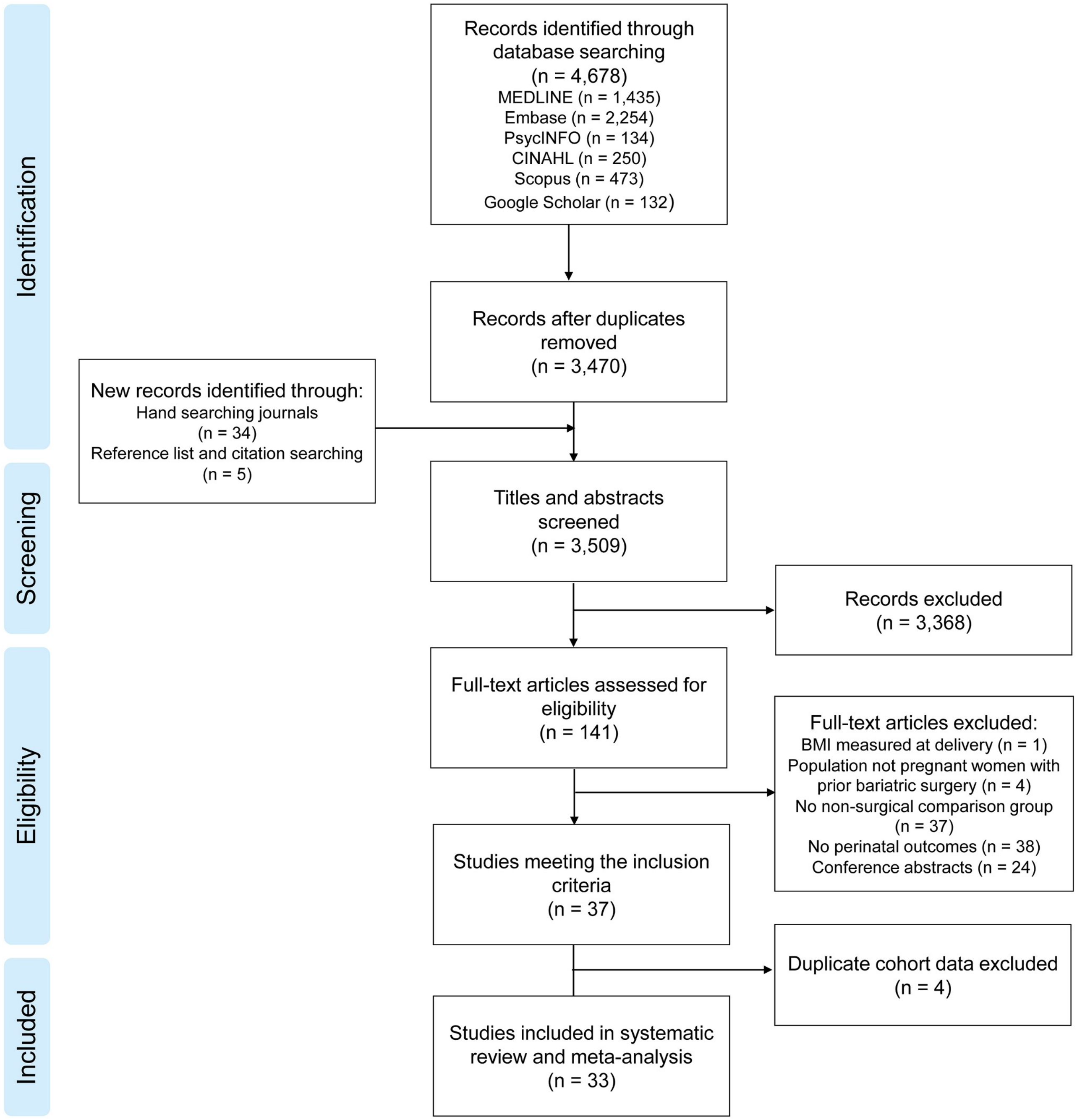

Fig 1. PRISMA flowchart of included studies. BMI, body mass index.

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general population controls (*n* = 656,353) [23]. Postterm birth was reported in five studies, and the odds more than halved after bariatric surgery (OR 0.46, 95% CI 0.35–0.60, $p < 0.001$) (Fig 3B) [22,37,44,50,51]. There was no significant heterogeneity ($I^2 = 7.2\%$, 95% CI 0.0–80.7, $p = 0.366$).

Despite the results of increased preterm birth and decreased postterm birth, the WMD of 13 studies reporting continuous gestational age did not reach statistical significance (WMD −0.16 weeks, 95% CI −0.38 to 0.06, $p = 0.156$) (S3 Fig) [22–24,30,33,36,38,40,41,44,49,51,52].

Table 1. Table of studies included in the systematic review and meta-analysis.

Author, publication year, country	Study period	Exposed groups*	Comparison groups*	Perinatal outcomes reported
Adams et al. 2015 [22], USA	Bariatric surgery between 1979 and 2011	(1) 764 pregnancies after RYGB (2) 2,666 pregnancies after RYGB	(1) 764 pregnancies matched for ppBMI (2) 10,447 pregnancies before RYGB	Birth weight Congenital anomalies Gestational age LGA Postterm birth Preterm birth Stillbirth SGA
Belogolovkin et al. 2012 [23], USA	Delivery between 2004 and 2007	293 pregnancies after bariatric surgery	656,353 general population pregnancies	Birth weight Gestational age Macrosomia Preterm birth SGA
Berglind et al. 2014 [24], Sweden	Bariatric surgery between 1980 and 2006	124 pregnancies after bariatric surgery	124 pregnancies before bariatric surgery	Birth weight Gestational age
Berlac et al. 2014 [25], Denmark	Bariatric surgery between January 1996 and June 2011	415 pregnancies after RYGB	827 pregnancies matched for ppBMI 829 healthy BMI 20–24 kg/m^2 pregnancies	Congenital anomalies NICU admission Stillbirth
Burke et al. 2010 [26], USA	Bariatric surgery between 2002 and 2006	354 pregnancies after bariatric surgery	346 pregnancies matched for presurgery BMI	LGA Stillbirth
Chevrot et al. 2016 [27], France	Delivery between January 1, 2004, and December 31, 2013	(1) 139 pregnancies after bariatric surgery (2) 58 pregnancies after RYGB (2) 81 pregnancies after LAGB or SG	(1) 139 pregnancies matched for presurgery BMI (2) 139 pregnancies matched for ppBMI	Birth weight LGA NICU admission Preterm birth SGA
Dell'Agnolo et al. 2011 [28], Brazil	Pregnancy between 1999 and 2008	41 pregnancies after bariatric surgery	14 pregnancies before bariatric surgery	Low birth weight Preterm birth
Dixon et al. 2005 [29], Australia	Bariatric surgery between January 1, 1995, and August 31, 2003	79 pregnancies after LAGB	79 pregnancies with obesity > 35 kg/m^2 40 pregnancies before LAGB 61,000 general population pregnancies	Birth weight Low birth weight Macrosomia Preterm birth
Ducarme et al. 2007 [30], France	Delivery between January 2004 and October 2006	13 pregnancies after LAGB	414 pregnancies with obesity > 30kg/m^2	Gestational age Low birth weight Macrosomia Preterm birth
Feichtinger et al. 2016 [31], Austria	Pregnancy between January 2007 and January 2016	76 pregnancies after RYGB	76 pregnancies with obesity > 30 kg/m^2 76 pregnancies matched for ppBMI 76 healthy BMI 18–25 kg/m^2 pregnancies	LGA NICU admission SGA
Gascoin et al. 2017 [9], France	Delivery between March 1, 2008, and October 31, 2012	56 pregnancies after RYGB	56 nonobesity pregnancies	Birth weight
Goldman et al. 2016 [32], USA	Bariatric surgery between 2002 and 2012	(1) 12 pregnancies after RYGB (2) 14 pregnancies after LAGB	(1)(2) 14 pregnancies with obesity (eligible for bariatric surgery) (1) 36 pregnancies before RYGB (2) 28 pregnancies before LAGB	Birth weight Preterm birth
Hammeken et al. 2017 [33], Denmark	Delivery between January 1, 2010, and December 31, 2013	151 pregnancies after RYGB	151 pregnancies matched for ppBMI	Birth weight Gestational age LGA NICU admission SGA
Johansson et al. 2015 [34], Sweden	Bariatric surgery between 2006 and 2011	596 pregnancies after bariatric surgery	2,356 pregnancies matched for presurgery BMI	Congenital anomalies LGA Preterm birth SGA Stillbirth

(*Continued*)

Table 1. (Continued)

Author, publication year, country	Study period	Exposed groups*	Comparison groups*	Perinatal outcomes reported
Josefsson et al. 2013 [35], Sweden	Mothers born between 1973 and 1983	318 pregnancies after bariatric surgery	244,294 general population pregnancies	Congenital anomalies
Josefsson et al. 2011 [36], Sweden	Mothers born between 1973 and 1983	126 pregnancies after bariatric surgery	188,500 general population pregnancies	Birth weight Gestational age LGA Preterm birth SGA
Kjaer et al. 2013 [37], Denmark	Delivery between January 2004 and December 2010	(1) 339 pregnancies after bariatric surgery (2) 286 pregnancies after RYGB	(1)(2) 1,277 pregnancies matched for ppBMI	LGA Postterm birth Preterm birth SGA
Lapolla et al. 2010 [38], Italy	Bariatric surgery between September 1993 and December 2005	(1) 83 pregnancies after LAGB (2) 27 pregnancies after LAGB	(1) 120 pregnancies with obesity > 40 kg/m^2 (1) 858 healthy BMI (criteria NR) pregnancies (2) 27 pregnancies before LAGB	Birth weight Gestational age LGA NICU admission Preterm birth SGA
Lesko and Peaceman 2012 [39], USA	Delivery between December 1, 2005, and December 1, 2009	70 pregnancies after bariatric surgery	140 pregnancies matched for presurgery BMI 140 pregnancies matched for ppBMI	Macrosomia NICU admission Preterm birth Stillbirth SGA
Machado et al. 2017 [40], Brazil	Pregnancy between March 2008 and March 2012	30 pregnancies after RYGB	60 pregnancies matched for ppBMI	Birth weight Gestational age SGA
Marceau et al. 2004 [41], Canada	Bariatric surgery before 2000	251 pregnancies after BPD	1,577 pregnancies before BPD	Birth weight Congenital anomalies Gestational age LGA SGA Stillbirth
Parent et al. 2017 [42], USA	Delivery between January 1, 1980, and May 30, 2013	1,859 pregnancies after bariatric surgery	8,437 general population pregnancies	Congenital anomalies LGA NICU admission Preterm birth SGA Stillbirth
Parker et al. 2016 [43], USA	Delivery in 2012	1,585 pregnancies after bariatric surgery	185,120 pregnancies with obesity > 30 kg/m^2	LGA SGA Stillbirth
Patel et al. 2008 [44], USA	Delivery between 2003 and 2006	26 pregnancies after RYGB	66 pregnancies with obesity > 30 kg/m^2 188 nonobesity BMI < 30 kg/ m^2pregnancies	Birth weight Congenital anomalies Gestational age Macrosomia Postterm birth Preterm birth SGA
Roos et al. 2013 [45], Sweden	Delivery between 1992 and 2009	2,534 pregnancies after bariatric surgery	12,468 pregnancies matched for ppBMI 1,740,140 general population pregnancies	LGA Preterm birth SGA Stillbirth
Rottenstreich et al. 2018 [46], Israel	Delivery between 2006 and 2016	119 pregnancies after SG	119 pregnancies matched for presurgery BMI	Congenital anomalies LGA NICU admission Preterm birth SGA

(*Continued*)

Table 1. (Continued)

Author, publication year, country	Study period	Exposed groups*	Comparison groups*	Perinatal outcomes reported
Shai et al. 2014 [47], Israel	Delivery between 1988 and 2010	326 pregnancies after bariatric surgery	1,612 pregnancies with obesity > 30 kg/m^2	Preterm birth
Skull et al. 2004 [48], Australia	Bariatric surgery between 1996 and 2003	49 pregnancies after LAGB	31 pregnancies before LAGB	Birth weight
Stentebjerg et al. 2017 [49], Denmark	Delivery between November 2007 and October 2013	71 pregnancies after RYGB	57,970 general population pregnancies	Birth weight Gestational age Preterm birth
Stephansson et al. 2018 [50], Sweden	Delivery between 1 January 2006 and 31 December 2013	1,431 pregnancies after bariatric surgery	4,476 pregnancies matched for presurgery BMI 798,338 general population pregnancies	Postterm birth
Wax et al. 2008 [51], USA	NR	38 pregnancies after RYGB	76 general population pregnancies	Birth weight Congenital anomalies Gestational age Macrosomia NICU admission Postterm birth Preterm birth SGA
Weintraub et al. 2008 [52], Israel	Delivery between 1988 and 2006	507 pregnancies after bariatric surgery	301 pregnancies before bariatric surgery	Birth weight Congenital anomalies Gestational age IUGR Macrosomia Stillbirth
Wittgrove et al. 1998 [53], USA	NR	36 pregnancies after RYGB	23 pregnancies before RYGB	Macrosomia Preterm birth

The term 'bariatric surgery' is used when a study combined all types of surgery or did not specify a surgery type.

*Some studies reported multiple exposed groups and multiple comparison groups. In the case of multiple exposed groups, numbers indicate which comparison group was used. There are no numbers when a single exposed group was compared to all listed comparison groups.

Abbreviations: BMI, body mass index; BPD, biliopancreatic diversion; IUGR, intrauterine growth restriction; LAGB, laparoscopic adjustable gastric banding; LGA, large for gestational age; NICU, neonatal intensive care unit; NR, not reported; ppBMI, prepregnancy BMI; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; SGA, small for gestational age.

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Heterogeneity between studies was substantial and did not reduce with subgroup analyses for type of bariatric surgery. Meta-regression revealed that the following factors did not contribute to heterogeneity: type of surgery, control group, publication year, continent, sample size, or quality score (S3A Table).

Size for gestational age and birth weight

SGA, intrauterine growth restriction, and low birth weight were investigated in 22 studies, and 21 of these were eligible for meta-analysis [22,27–31,33,34,36–46,51,52]. The odds of an SGA baby post-bariatric surgery were more than doubled (OR 2.13, 95% CI 1.80–2.52, $p < 0.001$) (S4 Fig). There was significant evidence of heterogeneity (I^2 = 47.0%, 95% CI 11.8–68.2, p = 0.009), which was reduced by subgroup analyses by surgery type (Fig 4A). Odds of SGA were significantly increased for the 'all bariatric surgery' group (OR 1.87, 95% CI 1.61–2.17, $p < 0.001$) and were further increased for 'RYGB or BPD' (OR 2.72, 95% CI 2.32–3.20, $p < 0.001$). There was no association between SGA and 'LAGB or SG' (OR 1.25, 95% CI 0.62–2.51, p = 0.533). The study excluded from the meta-analysis reported an adjusted OR of 2.69

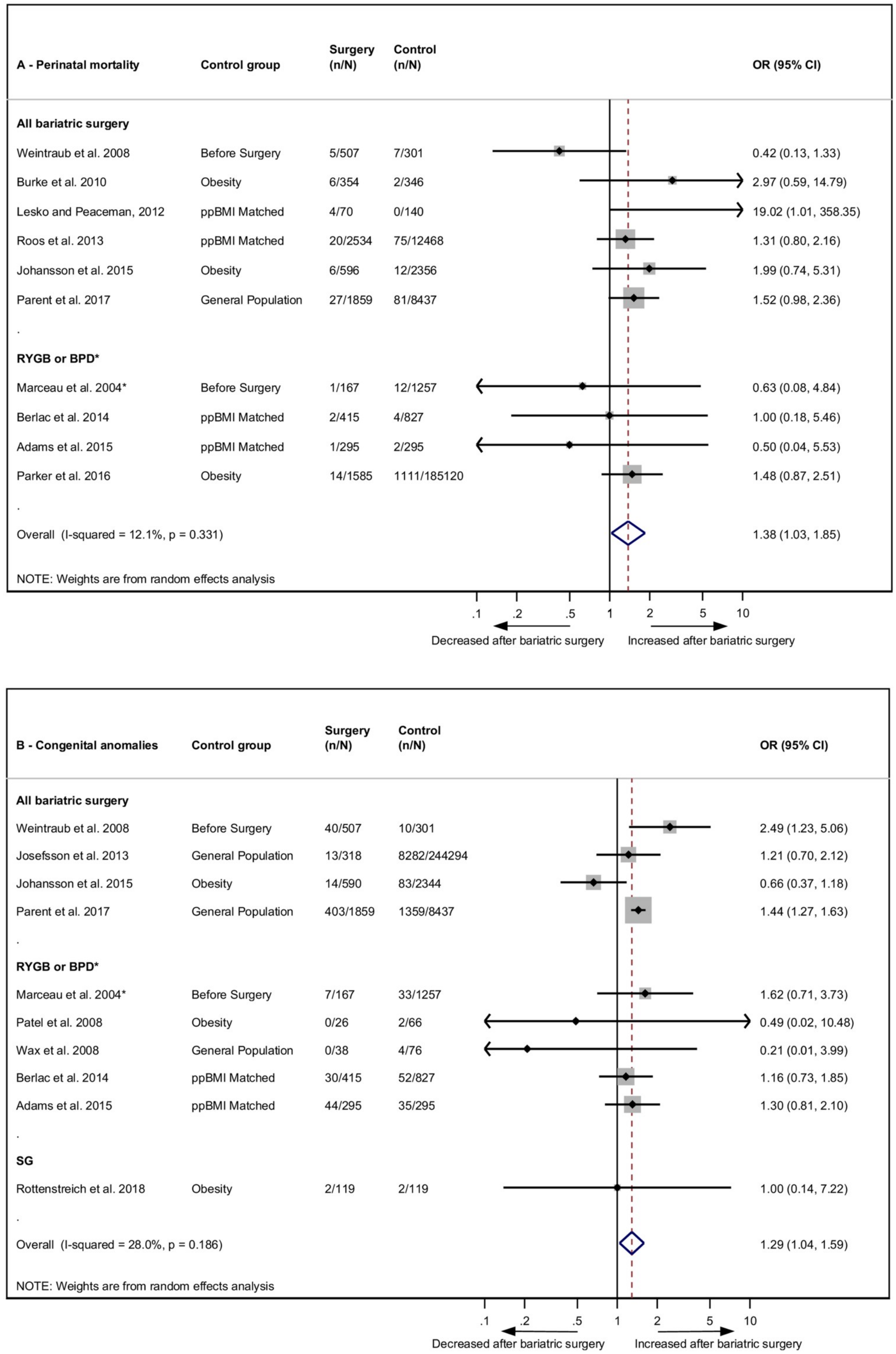

Fig 2. Perinatal mortality and congenital anomalies after bariatric surgery meta-analysis. Association between maternal bariatric surgery and (A) perinatal mortality (includes stillbirth) and (B) congenital anomalies. Studies are presented as Author, year. The forest plots are stratified by type of surgery. *n* = cases of perinatal mortality or congenital anomalies. *N* = total group size. *BPD only. BPD, biliopancreatic diversion; CI, confidence interval; OR, odds ratio; ppBMI, prepregnancy body mass index matched; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

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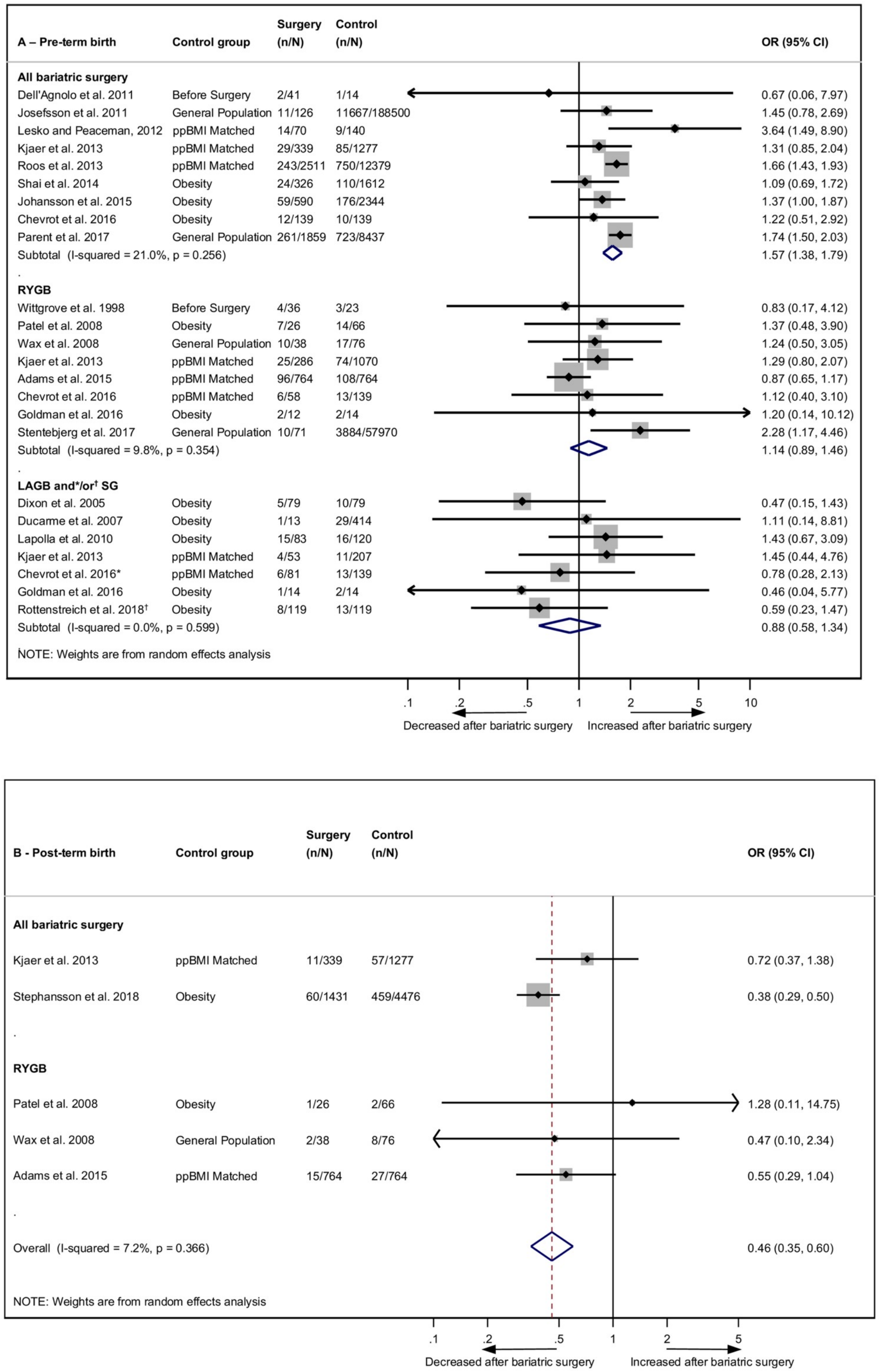

Fig 3. Preterm and postterm birth after bariatric surgery meta-analysis. Association between maternal bariatric surgery and (A) preterm birth (<37 weeks) and (B) postterm birth (>41 or >42 weeks). Studies are presented as Author, year. The forest plots are stratified by type of surgery, with separate pooled OR (95% CI) when subgroup analysis was possible. *n* = cases of preterm or postterm birth. *N* = total group size. *LAGB and SG. †SG only. CI, confidence interval; LAGB, laparoscopic adjustable gastric banding; OR, odds ratio; ppBMI, prepregnancy body mass index matched; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

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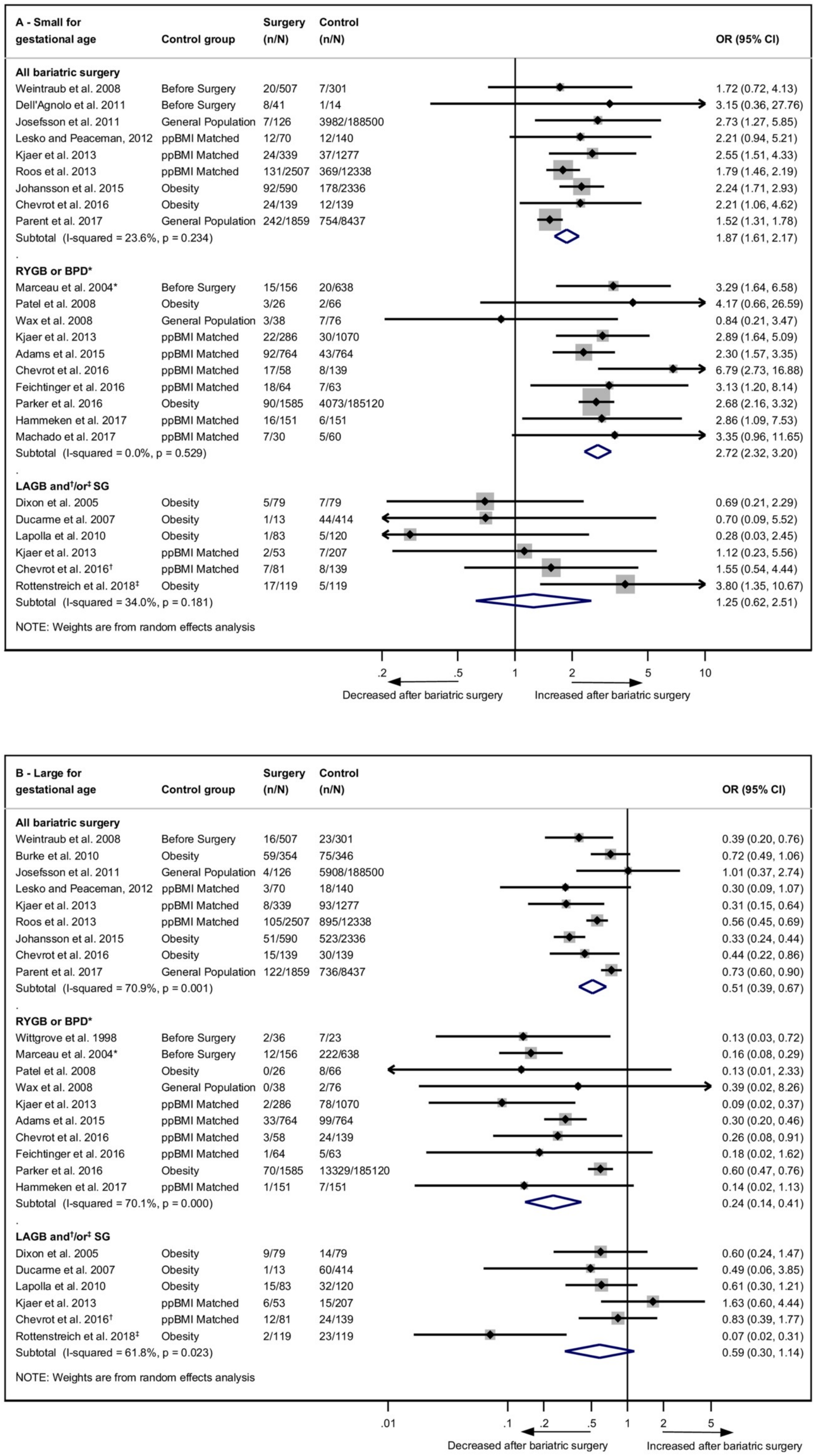

Fig 4. Size for gestational age after bariatric surgery meta-analysis. Association between maternal bariatric surgery and (A) small for gestational age (includes low birth weight < 2,500 g for three studies) and (B) large for gestational age (includes macrosomia > 4,000 g for seven studies). Studies are presented as Author, year. Results are subgrouped by type of surgery. n = cases of small or large for gestational age. N = total group size. *BPD only. †LAGB and SG. ‡SG only. BPD, biliopancreatic diversion; CI, confidence interval; LAGB, laparoscopic adjustable gastric banding; OR, odds ratio; ppBMI, prepregnancy body mass index matched; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

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(95% CI 1.96–3.69) post-bariatric surgery (n = 293) compared to general population controls (n = 656,353) [23].

LGA and macrosomia were investigated in 22 studies, and 21 were eligible for meta-analysis [22,26,27,29–31,33,34,36–39,41–46,51–53]. The ORs of an LGA baby post-bariatric surgery were more than halved (0.42, 95% CI 0.34–0.54, $p < 0.001$) (S5 Fig). There was substantial evidence of heterogeneity (I^2 = 69.5%, 95% CI 52.4–80.5, $p < 0.001$). Subgroup analyses by type of surgery identified that the 'RYGB or BPD' group was associated with the biggest decrease in odds of LGA (OR 0.24, 95% CI 0.14–0.41, $p < 0.001$), in comparison with 'all bariatric surgery' (OR 0.51, 95% CI 0.39–0.67, $p < 0.001$), and 'LAGB or SG', which was not significant (OR 0.59, 95% CI 0.30–1.14, p = 0.116) (Fig 4B). Heterogeneity did not decrease in these subgroup analyses. Meta-regression revealed that sample size was significantly contributing to heterogeneity (residual I^2 = 61.21, coefficient = 0.249, p = 0.031) (S3B Table). The study excluded from the meta-analysis reported an adjusted OR of 0.03 (95% CI 0.01–0.21) for LGA post-bariatric surgery (n = 293) compared to general population controls (n = 656,353) [23].

Birth weight mean and standard deviation for babies born after maternal bariatric surgery and controls were reported in 17 studies [9,22–24,27,29,32,33,36,38,40,41,44,48,49,51,52]. WMD was significantly lower post-bariatric surgery (WMD −242.42 g, 95% CI −307.43 g to −-177.40 g, $p < 0.001$) (S6 Fig). Heterogeneity was substantial (I^2 = 75.7%, 95% CI 61.1–84.8, $p < 0.001$) but reduced after subgroup analyses by surgery type. RYGB resulted in the largest reduction in birth weight (WMD −226.10 g, 95% CI −273.43 g to −178.78 g, $p < 0.001$), compared with 'all bariatric surgery' (WMD −223.71 g, 95% CI −273.68 g to −173.74 g, $p < 0.001$), and 'LAGB', for which the reduction was not significant (WMD −135.14 g, 95% CI −289.17 g to 18.90 g, p = 0.086). One study investigated only BPD, for which the mean difference was −500 g (95% CI −570.85 g to −429.15 g, $p < 0.001$).

NICU admission

NICU admission was reported in nine studies with babies born post-bariatric surgery being significantly more likely to be admitted to NICU (OR 1.41, 95% CI 1.25–1.59, $p < 0.001$) (Fig 5) [25,27,31,33,38,39,42,46,51]. There was no evidence of heterogeneity (I^2 = 0.0%, 95% CI 0.0–64.8, p = 0.808).

Publication bias and sensitivity analyses

There was no evidence of small study effects for any outcome except LGA (p = 0.021), which may signal publication bias (S7 Fig, S4 Table). A subset of studies reported both crude and adjusted data for the adverse perinatal outcomes, but when compared, there was little difference in size or direction of associations (S8 Fig). Sensitivity analyses revealed that the results were robust, with only small changes in pooled effect sizes when meta-analysis were repeated with one study excluded (S5 Table).

Discussion

This systematic review and meta-analysis has demonstrated that perinatal mortality, congenital anomalies, preterm birth, SGA, and NICU admission are associated with increased odds in women who have had bariatric surgery prior to pregnancy compared to women without prior bariatric surgery. Postterm birth and LGA, however, are associated with decreased odds after bariatric surgery. Malabsorptive procedures were associated with a significant increase in SGA and decrease in LGA, whereas restrictive procedures were not. Subgrouping by type of surgery significantly reduced heterogeneity for the outcomes with a high I^2 value, whereas

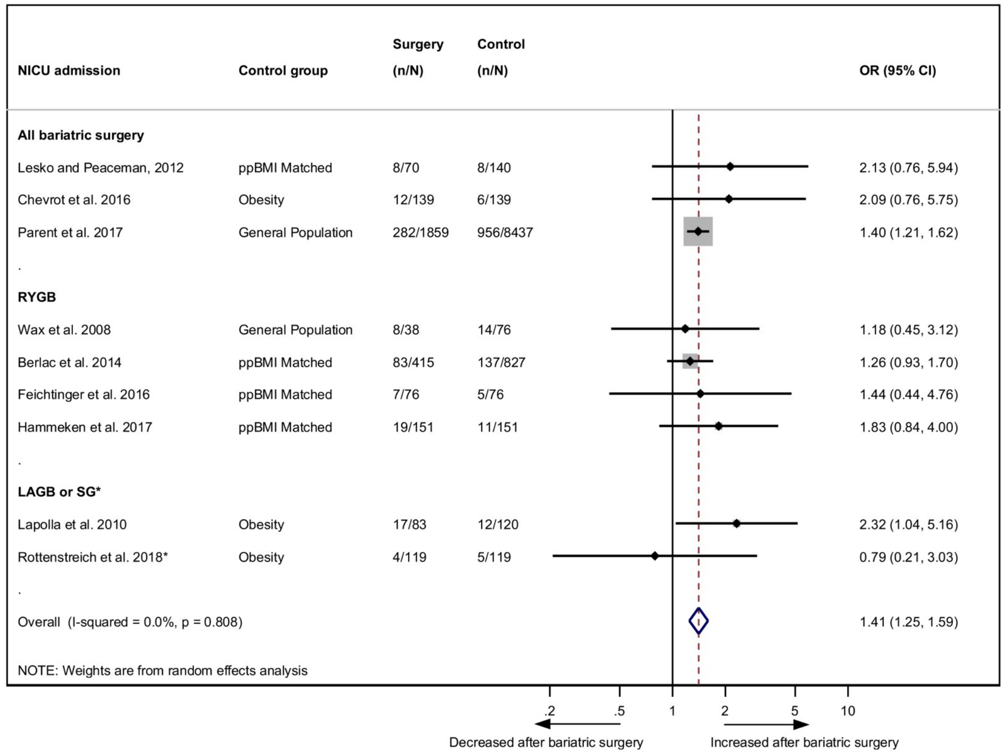

Fig 5. NICU admission after bariatric surgery meta-analysis. Association between maternal bariatric surgery and NICU admission. Studies are presented as Author, year. The forest plot is stratified by type of surgery. *n* = cases of NICU admission. *N* = total group size. *SG only. CI, confidence interval; LAGB, laparoscopic adjustable gastric banding; NICU, neonatal intensive care unit; OR, odds ratio; ppBMI, prepregnancy BMI matched; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

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subgrouping by control group did not. There was no evidence of publication bias for any outcome except LGA.

The increase in adverse perinatal outcomes could be related to malnutrition. Unlike restrictive procedures, which reduce stomach size and appetite, malabsorptive procedures bypass a portion of the small intestine where many vitamins and minerals are absorbed, making these patients particularly susceptible to nutrient deficiencies that may negatively affect a subsequent pregnancy [54]. The association between folic acid intake and neural tube defects is well established, and there are links between iron deficiency and preterm birth and between calcium and birth weight [55–57]. Impaired nutrient transport across the placenta is also associated with perinatal morbidity; however, there is limited evidence regarding placental function after bariatric surgery. The studies reporting data on congenital anomalies in pregnancy with and without prior bariatric surgery did not subgroup by type of anomaly—this would be valuable for future research to pinpoint the mechanism behind the anomalies. Another factor that may explain the increase in SGA infants is the increased glycaemic variability and postprandial hypoglycaemia observed after RYGB, as fetal growth has been found to be associated with maternal glucose nadir levels during oral glucose tolerance testing in pregnancy [58].

The strengths of this systematic review and meta-analysis include the thorough search strategy of multiple databases and supplementing this with hand searches of reference lists, citations, and relevant journals. All screening, data extraction, and quality assessment was carried out in duplicate to minimise human error. There are no randomised controlled trials, because of the nature of this research question, but all included studies were medium- to high-quality observational studies. This is the first meta-analysis, to our knowledge, to report significantly increased odds of perinatal mortality and congenital anomalies after bariatric surgery. This is also the first meta-analysis, to our knowledge, to investigate postterm birth after bariatric surgery, for which a significant decrease was found. The results for SGA, LGA, preterm birth, and NICU admission confirm the findings of past meta-analyses but with stronger associations than previously reported and the inclusion of 12 additional studies [9,22,24,27,28,32,33,40,42,46,49,50].

The results from our study are limited by the small sample sizes of some of the included studies. Multiple studies reported few, or even zero, cases of perinatal mortality or congenital anomalies and have therefore resulted in large CIs. Larger epidemiological studies or individual patient data (IPD) meta-analyses need to be carried out for this rare exposure and rare outcome combination. Additionally, there are no large studies exploring congenital anomalies and perinatal mortality specifically after restrictive surgery such as LAGB or SG, which may not have a detrimental effect. A number of studies have reported several adverse perinatal outcomes, many of which are linked, which may result in a loss of statistical and clinical independence. We were unable to include non–English language studies, and one non–English language study meeting our inclusion criteria was excluded. This study from France identified a significant decrease in macrosomia, as our meta-analysis did; however, it also found a decrease in SGA in contrast to the significant increase we found [59].

Women that become pregnant post-bariatric surgery tend to be older than the general population of pregnant women [7]. Many women also still have a BMI > 30 kg/m^2 despite the weight loss from surgery [45]. There is also evidence that alcohol use and smoking are increased after bariatric surgery [60]. The combination of increased maternal age, high BMI, and unhealthy behaviours in women after bariatric surgery plays a role in the development of adverse perinatal outcomes, in addition to the malnutrition. These are important confounders to consider when investigating perinatal outcomes in this group. When comparing ORs with adjustments made for these factors to unadjusted ORs, we did not see a change in the results. However, in a clinical setting, these factors and behaviours are important for the healthcare provider to take into account because of the evidence of the link with adverse perinatal outcomes. As with all meta-analyses of observational data, unmeasured confounding in the included studies may have implications on the results. Gestational weight gain (GWG) is another factor associated with perinatal outcomes such as birth weight; however, further research is required to determine how the relationship between GWG and pregnancy outcomes differs for women after bariatric surgery and whether current GWG guidelines can apply to this population.

The LAGB subgroup analyses tended to have larger CIs than any other subgroup. This may be due to smaller sample sizes or differences in LAGB band management. Some clinics actively manage gastric bands during pregnancy by deflating in cases of nausea or vomiting and inflating in cases of excess GWG [29]. Future studies should explore how band management could be used to achieve optimal pregnancy outcomes. The studies that combined all types of bariatric surgery drastically differed in surgery type composition, with studies reporting from 13.3% RYGB to 98% RYGB in their cohorts. It would be useful for future studies to separate outcomes by type of surgery or to conduct IPD meta-analyses on the existing data, which would enable standardisation of categories across studies.

Future studies should explore the effect of time to conception after different types of bariatric surgery, especially considering gestational weight loss and advanced maternal age. Many women that are previously considered to be infertile experience increased fertility after bariatric surgery, which may result in unexpected pregnancies immediately after surgery in the rapid weight loss phase [61]. Many clinics recommend waiting 12–18 months to conceive post-surgery, but the evidence base is limited for this.

Bariatric surgery prior to pregnancy is promising for reducing obesity-related comorbidities for the mother, and benefits include reduced risks of gestational diabetes and preeclampsia, which are both serious complications associated with adverse maternal and fetal outcomes. Our meta-analysis has shown that the risks of postterm birth and LGA babies are reduced after bariatric surgery; however, we have also identified adverse outcomes for the baby and efforts now need to be focused on how to reduce these. Internationally, guidelines exist for a variety of high-risk pregnancy groups such as those with diabetes, hypertension, and obesity. This study confirms that bariatric surgery patients that become pregnant are also a high-risk group, and guidelines for health professionals need to be developed as obesity and bariatric surgery increases. The current evidence base could be used to inform risk communication about potential future pregnancies with women of reproductive age prior to surgery. For women with a history of bariatric surgery, preconception nutritional support should be offered, and increased fetal, nutrition, and glucose monitoring is required throughout pregnancy. Further studies are required to determine whether restrictive surgery results in better perinatal outcomes than malabsorptive surgery without compromising maternal outcomes, and if so, these may be the preferred surgery for women of reproductive age.

Supporting information

S1 Table. Search strategy for electronic databases and e-journals.
(DOCX)

S2 Table. Quality assessment scores for included studies.
(DOCX)

S3 Table. Meta-regression for outcomes with significant heterogeneity between studies.
(DOCX)

S4 Table. Eggers test of publication bias for perinatal outcomes after bariatric surgery.
(DOCX)

S5 Table. Sensitivity analyses for perinatal outcomes after bariatric surgery.
(DOCX)

S1 PRISMA Checklist. PRISMA checklist for systematic reviews and meta-analyses.
(DOC)

S1 Fig. Adapted Newcastle-Ottawa quality assessment scale for cohort studies.
(DOCX)

S2 Fig. Preterm birth after bariatric surgery meta-analysis.
(DOCX)

S3 Fig. Gestational age (weeks) after bariatric surgery meta-analysis with subtotals by type of surgery.
(DOCX)

S4 Fig. Small for gestational age after bariatric surgery meta-analysis.
(DOCX)

S5 Fig. Large for gestational age after bariatric surgery meta-analysis.
(DOCX)

S6 Fig. Birth weight (grams) after bariatric surgery meta-analysis with subtotals by type of surgery.
(DOCX)

S7 Fig. Funnel plots of publication bias for perinatal outcomes after bariatric surgery.
(DOCX)

S8 Fig. Crude versus adjusted data for studies reporting adjusted odds ratios.
(DOCX)

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BARIATRIC SURGERY/PREGNANCY

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Pregnancy after bariatric surgery: Consensus recommendations for periconception, antenatal and postnatal care

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Summary

The objective of the study is to provide evidence-based guidance on nutritional management and optimal care for pregnancy after bariatric surgery. A consensus meeting of international and multidisciplinary experts was held to identify relevant research questions in relation to pregnancy after bariatric surgery. A systematic search of available literature was performed, and the ADAPTE protocol for guideline development

Abbreviations: ADA, American Diabetes Association; AGB, Adjustable gastric band; BMI, Body mass index; BPD, Biliopancreatic diversion; BS, Bariatric surgery; CBG, Capillary blood glucose; CGM, Continuous glucose monitoring; COC, Combined oral contraception; FGR, Fetal growth restriction; FPG, Fasting plasma glucose; GDM, Gestational diabetes mellitus; GI, Glycaemic index; GWG, Gestational weight gain; INR, International normalized ratio; IOM, Institute of Medicine; IUD, Intrauterine device; IUS, Intrauterine system; LARC, Long-acting reversible contraception; LGA, Large for gestational age; NICU, Neonatal intensive care unit; OGTT, Oral glucose tolerance testing; PHH, Postprandial hyperinsulinaemic hypoglycaemia; PTH, Parathyroid hormone; RYGB, Roux-en-Y gastric bypass; SG, Sleeve gastrectomy; SGA, Small for gestational age; T2DM, Type 2 diabetes; WHO, World Health Organization

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followed. All available evidence was graded and further discussed during group meetings to formulate recommendations. Where evidence of sufficient quality was lacking, the group made consensus recommendations based on expert clinical experience. The main outcome measures are timing of pregnancy, contraceptive choice, nutritional advice and supplementation, clinical follow-up of pregnancy, and breastfeeding. We provide recommendations for periconception, antenatal, and postnatal care for women following surgery. These recommendations are summarized in a table and print-friendly format. Women of reproductive age with a history of bariatric surgery should receive specialized care regarding their reproductive health. Many recommendations are not supported by high-quality evidence and warrant further research. These areas are highlighted in the paper.

KEYWORDS

bariatric surgery, metabolic surgery, obesity, pregnancy, obstetrics, gynaecology

1 | INTRODUCTION

The prevalence of obesity worldwide has nearly tripled between 1975 and 2016. In 2016, 1.9 billion adults aged 18 years or older (40% of women and 39% of men) were affected by overweight (BMI 25-29 kg/m^2) with 650 million (11% men and 15% women) having obesity (BMI $\geq$ 30 kg/m^2).[1] Obesity increases complications for both mother and offspring during pregnancy and childbirth.[2] Furthermore, there is growing evidence that parental nutrition and lifestyle affect embryonic development with potential long-term health implications for the infant through on the process of developmental programming.[3,4] As such, it is generally recommended that both women and men with obesity lose weight before conception.[5,6] Based on international guidelines,[7] patients with class III obesity (BMI $\geq$ 40 kg/m^2) or class II obesity (BMI 35-39 kg/m^2) with associated comorbidities may be eligible for bariatric surgery (BS). Poor success with weight loss by diet alone has led to BS becoming increasingly popular.[8] Common procedures include (1) sleeve gastrectomy (SG), the most frequently performed operation,[9] in which the greater curvature of the stomach is resected, reducing stomach volume by 75%, thus limiting food intake. This procedure also removes ghrelin-producing secreting endocrine cells present in the greater curvature of the stomach, which aid in appetite reduction. Weight loss as well as alterations in other metabolic hormones results in the improvement of glucose homeostasis and results in positive effects on comorbidities therefore reducing appetite and aiding in subsequent diabetes remission.[10] (2) Roux-en-Y gastric bypass (RYGB), a mixed procedure in which the volume of the stomach is reduced to approximately 15 to 30 mL and the absorption of nutrients, is impaired by bypassing part of the small intestine and diverting the food flow to the distant small intestine. This approach not only results in a limited oral intake but also induces malabsorption, although this is reduced over time because of intestinal hypertrophy. Furthermore, an increase in gut hormone secretion (including GLP-1 and PYY) hormones associated with RYGB may diminish appetite and result in better glucose homeostasis.[11] (3) Adjustable gastric band (AGB) procedures where an inflatable restrictive band is placed around the upper portion of the stomach creating a small pouch with a narrow opening to the lower stomach, adjusted by adding or removing fluid to the band via a subdermal port. This reduces stomach capacity and appetite.[12] Other types of surgery include biliopancreatic diversion with duodenal switch, intragastric balloon, and vertical banded gastroplasty, but these are outdated or rarely performed.

As a result of weight loss and enteroendocrine alteration, BS has also been shown to reduce the incidence of obesity-related comorbidities and complications.[13] BS is however associated with a potential increase in adverse events due to surgical complications and micronutrient deficiencies and derangements in (neuro)endocrine and metabolic homeostasis.[14-17] Approximately 80% of BS is in women, many of whom are of reproductive age.[18-20] BS may improve fertility through restoration of ovulation, and pregnancies after BS are becoming increasingly common.[21] It has been recognized that changes in gut anatomy and physiology with potential for malnutrition incur increased potential for adverse perinatal outcomes such as small for gestational age (SGA), preterm birth, congenital abnormalities, and perinatal mortality. Pregnancy soon after surgery may increase risk of maternal morbidity and/or mortality.[22]

A need for more specific guidance and nutritional management was recognized, and an international group of experts was assembled to review the available evidence and provide recommendations on the periconception, antenatal, and postnatal care of pregnancies after BS.

2 | METHODS

An expert meeting focused on pregnancy after BS was organized at the University of Surrey, UK in April 2017 with a follow-up meeting at University Hospital Leuven, Belgium, in November 2017. These meetings brought together national and international expertise from a multidisciplinary group of researchers and clinicians including specialists in obstetrics and gynaecology, bariatric surgery, endocrinology, dietetics, nutrition, nursing and midwifery, health psychology, epidemiology, and public health. Additional international colleagues were able to join both meetings through teleconferencing.

The objectives of the meetings were to discuss the key questions, to advance scientific knowledge and practice in the area of pregnancy after BS, and to identify key areas of focus for collaborative work to produce consensus clinical guidelines on best practice for facilitating healthy pregnancies after BS.

The clinical guideline was developed using the structure from ADAPTE.[23] The group formulated specific clinical questions in relation to pregnancy after BS (Table 1). For each question, a systematic search of the available literature was performed, identifying articles published from inception to July 2018. Search terms related to pregnancy ("pregnancy," "prepregnancy," "mother," "maternal," "conception," "preconception," "gravid," "pregravid") were combined with terms related to BS ("bariatric surgery," "weight loss surgery," "gastric bypass," "Roux-en-Y," "RYGB," "sleeve gastrectomy," "gastric sleeve," "gastroplasty," "gastric band," "LAGB," "biliopancreatic diversion," "BPD," "duodenal switch") and terms specific for each clinical question. Articles resulting from these searches and relevant references cited in those articles were reviewed. All evidence was graded (Table 2)[24] and discussed during group meetings. When evidence of sufficient quality was lacking, the group made consensus recommendations based on expert clinical experience. Consensus on the guidelines was declared when 100% of the group agreed with the recommendations. The final document was reviewed by all authors. The recommendations made by this group are summarized in Table 3.

3 | EVIDENCE AND RECOMMENDATIONS

3.1 | Bariatric surgery to conception interval

The period after BS is characterized by weight loss which may be rapid after SG and RYGB procedures and slower after AGB, once optimal adjustment has been achieved. During this period postsurgery,[25,26] women are recommended to postpone pregnancy in order to ensure maximal weight loss, weight stabilization, and to reduce the risk of macronutrient and micronutrient deficiencies and electrolyte imbalances.[5] Evidence in regard to this recommendation is however scarce. We identified 14 studies reporting on the surgery-to-conception interval and pregnancy outcomes, but many studies have limitations in methodology thus preventing comparison.

TABLE 1 Clinical questions to be answered in this guideline

Clinical Questions to be Answered in This Guideline
What is the recommended time interval between bariatric surgery and conception?
What types of contraception should be advised to women after bariatric surgery?
Are there special recommendations regarding dietary behaviour?
Which micronutrients should be monitored? Which types of supplements should be prescribed?
Should patients be screened for gestational diabetes and how should they be screened?
Which medical and surgical complications should be monitored, and can they be prevented?
Is breastmilk composition affected by bariatric surgery and can it safely be recommended to patients?

TABLE 2 Type and level of evidence[24]

Quality and Level of Evidence	
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs (including cluster RCTs) with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs (including cluster RCTs) with a low risk of bias
1−	Meta-analyses, systematic reviews of RCTs, or RCTs (including cluster RCTs) with a high risk of bias
2++	High-quality systematic reviews of these types of studies, or individual, non-RCTs, case-control studies, cohort studies, CBA studies, ITS, and correlation studies with a very low risk of confounding, bias or chance, and a high probability that the relationship is causal
2+	Well-conducted non-RCTs, case-control studies, cohort studies, CBA studies, ITS, and correlation studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2−	Non-RCTs, case-control studies, cohort studies, CBA studies, ITS and correlation studies with a high risk—or chance—of confounding bias, and a significant risk that the relationship is not causal
3	Non-analytic studies (for example, case reports, case series)
4	Expert opinion, formal consensus

Parent et al[22] found that a shorter surgery-to-birth interval (less than 2 years) was associated with a higher risk for prematurity, SGA, and neonatal intensive care unit (NICU) admission (level 2++), but data on long-term outcomes were missing. In contrast, Stentebjerg et al[27] and Nomura et al[28] found an increased risk for certain pregnancy complications (iron deficiency, excessive gestational weight gain (GWG), and delivery by caesarean section) if the pregnancy was postponed according to this recommendation (level 2+). Norgaard et al[29] found no difference in the prevalence of SGA prior to, or after, 18 months (level 2++). Other studies also did not find a difference in gestational outcomes according to surgery to conception interval.[27,30-37]

Based on level 2++ evidence, the members of this group recommend postponing pregnancy until a stable weight is achieved. This is typically achieved 1 year after SG or RYGB procedures and 2 years after AGB.

3.2 | Contraception

Women recommended to postpone pregnancy during the period of rapid weight loss (1-2 years) require adequate counselling regarding safe and effective contraception.[38] As obesity is associated with impaired fertility due to metabolic syndrome and PCOS, patients

TABLE 3 Recommendations for clinical practice

Summary of Recommendations	Periconception	First Trimester	Second Trimester	Third Trimester	Postpartum/Breastfeeding
Surgery-to-conception interval	Postpone pregnancy until a stable weight is achieved (level 2++)				
Contraception	Counsel women regarding contraception prior to surgery (level 2−) Avoid COCs (level 2+), and encourage the use of LARCs (level 2−)				Counsel women regarding contraception (level 2−) Avoid COCs (level 2+), and encourage the use of LARCs (level 2−)
Nutritional advice	Energy requirements should be individualized on the basis of prepregnancy BMI, GWG, and physical activity level, with limitations on energy dense foods if excessive GWG is identified (level 2−) Provide standard postsurgical dietary advice (level 4) Aim for protein intakes of at least 60 g/day (level 4) Where deranged glucose levels are identified (hyperglycaemia or hypoglycaemia) manipulation of carbohydrate quantity, and/or quality may be warranted (level 4) Hyperglycaemia—reduce rapidly absorbed carbohydrates. Substitute with protein and low GI alternatives (level 4) Early or late dumping—eliminate rapidly absorbed carbohydrates. Substitute with protein and low GI alternatives, six smaller meals. Use liquids 30 min after meals and lay down after eating (level 2−). Avoid caffeinated or alcoholic beverages (level 4) and consider changing eating frequency and portion size (level 4). Artificial nutrition support may be indicated in cases of severe malnutrition during pregnancy, with initiation and choice of feeding route determined by local nutrition support protocols (level 4)				
Nutritional monitoring	Serum indices to be checked every 3 months: full blood count, serum ferritin, and iron studies including transferrin saturation (level 2−), serum folate or red blood cell folate, serum vitamin B12 or transcobalamin (level 2−), serum vitamin A (level 2−). Serum indices to be checked every 6 months: prothrombin time, INR, and serum vitamin K1 concentration (level 2+), serum protein and albumin (level 2−), serum vitamin D with calcium, phosphate, magnesium, and PTH (level 4), renal function and liver function tests (level 4), serum vitamin E	Serum indices to be checked every trimester: full blood count, serum ferritin, and iron studies including transferrin saturation (level 2−), serum folate, and serum vitamin B12 (level 2−), serum vitamin A (level 2−), prothrombin time, INR, and serum vitamin K1 concentration (level 2+), serum protein and albumin (level 2−), serum vitamin D with calcium, phosphate, magnesium, and PTH (level 4), renal function and liver function tests (level 4) Extra serum indices to be checked during first trimester: serum vitamin E (level 4), serum zinc, copper, and selenium (level 4).			Serum indices to be checked every 3 months while breastfeeding: full blood count, serum ferritin, and iron studies including transferrin saturation (level 2−), serum folate, and serum vitamin B12 (level 2−), serum vitamin A (level 2−), serum vitamin D with calcium, phosphate, magnesium, and PTH (level 4). Serum indices to be checked every 6 months while breastfeeding: prothrombin time, INR, and serum vitamin K1 concentration (level 2+), serum protein and albumin (level 2−), renal function

(Continues)

TABLE 3 (Continued)

Summary of Recommendations	Periconception	First Trimester	Second Trimester	Third Trimester	Postpartum/Breastfeeding
	(level 4), serum zinc, copper, and selenium (level 4).				and liver function tests (level 4), serum vitamin E (level 4), serum zinc, copper, and selenium (level 4).
Nutritional supplementation	Prepregnancy multivitamin and mineral supplement to ensure total daily dosing from all supplements, eg, Table 3 (level 4). Folic acid 0.4 mg daily during preconception and first trimester, 4-5 mg if obese or diabetic (level 4). Convert Vitamin A to beta-carotene form (level 2+). Add oral dose of vitamin K weekly if deficiency is noted with coagulation defect (level 2−). Vitamin B12 supplementation (1 mg IM 3 monthly) (level 4). Oral supplementation can be attempted, but reduced absorption is to be expected (level 4). Supplement vitamin D to keep levels above 50 nmol/L, and serum PTH within normal levels (level 4). Add calcium as needed (level 4). Additional supplementation should be given if deficiency is identified.	Thiamine 300 mg daily with two vitamin B compound strong tablets three times daily if vomiting. Prolonged vomiting may require intravenous thiamine and vitamin B complex supplementation (level 3). Give folic acid at a dose of 0.4 mg daily during preconception and first trimester, 4-5 mg if obese or diabetic (level 4). Further supplementation as during preconception period.			
Diabetes screening	Monitor HbA1c every 3 months in the absence of haemoglobinopathies.	Check fasting glucose/HbA1c if there is a personal history of diabetes or if other risk factors are	OGTT at 24-28 weeks for women who have had AGB (level 4). For all other women either seven-point	Repeat screening if clinical suspicion of diabetes (level 4).	Offer screening to patients with GDM. Screen other patients according to local policies or as

(Continues)

TABLE 3 (Continued)

Summary of Recommendations	Periconception	First Trimester	Second Trimester	Third Trimester	Postpartum/Breastfeeding
	If haemoglobin is abnormal then monitor with fasting glucose +/− OGTT. Less frequent testing can be considered if the woman does not have a history of diabetes, according to local policies (level 4).	present. Treat as T2DM if HbA1c ≥6.5% and/or FPG ≥7.0 mmol/L (level 4).	CBG profiles or CGM for 1 week between 24 and 28 weeks of gestation (level 4). Repeat HbA1c if there is a personal history of diabetes (level 4).		clinically indicated (level 4).
AGB management		Deflate in case of hyperemesis to prevent band slippage and nutrient deficiencies (level 3).	Assess GWG and fetal growth and manage band as appropriate (level 2++).	Assess GWG and fetal growth and manage band as appropriate (level 2++).	After establishment of lactation, return band to prepregnancy levels (level 2+).
Surgical complications	Excess vomiting—AGB deflation in symptomatic women only to prevent band slippage and/or nutrient requirements not being met (level 3). In case of RYGB, patients should seek medical attention upon onset of abdominal symptoms—timely recognition and early surgical intervention of internal herniation is associated with reduced risk of adverse maternal and fetal outcomes (level 2++).				
Weight management	Postpone pregnancy until a stable weight is achieved (level 2++). Measure preconception weight (level 4).	Measure maternal weight (level 4).	Measure maternal weight and assess for excessive or inadequate GWG. If excessive GWG, assess for complications (level 2+). If ABG, assess GWG and fetal growth and manage band as appropriate (level 2++). If insufficient GWG, monitor fetal growth carefully (level 4)		Pregnancy does not affect long-term weight loss from BS (level 2+).
Ultrasound scans		Perform routine 12-week scan (routine) (level 4).	AGB should be deflated if fetal growth is compromised (level 2++). Perform routine 20-week scan congenital anomaly screening (level 4).	Perform monthly fetal growth monitoring scan(s) from viability (level 2+). Assess for developmental problems such as intracranial bleeding (level 3).	
Mental health	Screen for substance abuse and anxiety or other mental health disorders and offer follow-up if necessary (level 2+). Advise smoking cessation if necessary (level 2−).				
Breastfeeding					Breastfeeding can be recommended to bariatric patients (level 2++). Monitor maternal micronutrients during lactation (level 3).

Abbreviations: COC, combined oral contraceptive; LARC, long-acting reversible contraception; BMI, body mass index; GWG, gestational weight gain; GI, glycaemic index; PTH, parathyroid hormone; OGTT, oral glucose tolerance test; AGB, adjustable gastric banding; CBG, capillary blood glucose; CGM, continuous glucose monitoring.

may not be using contraception presurgery. They should be made aware that fertility increases postoperatively, and contraception usage should be discussed (level 2+).[39] There is sufficient evidence to show that perioperative contraceptive counselling increases the postoperative use of contraception (level 2+).[40,41] Contraceptive counselling and contraceptive knowledge by health care providers could however be improved (level 2−),[42,43] as contraceptive use after BS is often suboptimal, with many women using least reliable methods (level 2+).[39,40,44-48] This is even more important in patients with a history of infertility, as they have been found to be at increased risk for unprotected intercourse without intent to conceive and have higher early postoperative conception rates.[39]

Both RYGB and, to a lesser extent, SG significantly alter the anatomical structure of the gastrointestinal tract, and theoretically, this gut shortening could affect the absorption of oral contraceptives containing an oestrogen component which undergoes metabolism in the upper gut wall. Absorption of ethinylestradiol from the contraceptive pill may be reduced leading to a decrease in efficacy.[49] Reliability might also decrease due to postoperative side effects and complications such as vomiting and/or diarrhoea; however, there are few data in women after BS. Limited clinical evidence suggests no substantial decrease in effectiveness of oral contraception among women who underwent a biliopancreatic diversion (BPD), a now uncommon procedure, or AGB.[50,51] However, evidence from pharmacokinetic studies has shown increased contraceptive failure for progestogen oral contraception among women who underwent a jejunoileal bypass (an older procedure).[52,53] In general, combined oral contraception (COC) may be less reliable after BS (level 2+).[51] Additionally, many individuals are still affected by obesity after BS, and this represents a relative contraindication for the use of COC, with both factors increasing the risk of venous thromboembolism.[38] Alternatives found to be unaffected by BS are parenteral long-acting reversible contraception (LARC) methods such as the copper intrauterine device (IUD), intrauterine systems (IUS), and progestogen implants. They have been found to be highly effective and acceptable to women (level 2−).[54-57] For women choosing nonhormonal barrier methods, both male and female condoms may be suitable; however, the contraceptive diaphragm may be difficult to insert correctly and less reliable as it requires refitting after every 3 kg of weight change.[58]

Consensus from available evidence is that women should receive counselling regarding contraception prior to surgery (level 2−). Combined oral contraception containing oestrogen should be avoided after BS (level 2+). The use of long-acting reversible contraception such as implants, IUD, or IUS should be encouraged and offered as first line following BS (level 2−).

4 | NUTRITION AND MICRONUTRIENT MONITORING

4.1 | Nutritional advice

A large proportion of pregnant women have a poor diet,[59] independent of BS history. The focus should remain on the regular monitoring of diet quality and nutritional status and on encouraging a general healthy dietary pattern and lifestyle.[3] At the same time, a healthy diet post-BS may differ in food group proportions from that of the nonsurgical pregnant population. This is due to a greater emphasis on lean protein sources, followed by fruit and vegetables, and lastly starchy carbohydrates, as the main component of the post BS diet. There is little or no evidence-based specific dietary (food-based) advice for pregnancies post BS and few published reports of the dietary intakes of this population.[60] It therefore seems prudent to combine what we know about an appropriate postsurgical diet with the accepted general dietary advice for pregnancy to provide appropriate guidance.

Energy requirements should be individualized on the basis of prepregnancy BMI, GWG, and physical activity level, with limitations on energy-dense foods if excessive GWG is identified (level 2+).[60] Beard et al[61] recommend a minimum of 60 g of protein/day during pregnancy post-BS (level 4). However, subsequent antenatal achievement of protein requirements is more difficult following bypass operations.[62] In the nonpregnant postsurgical patient, intakes of up to 1.5 g/kg ideal body weight/day are proposed (up to a maximum of 2.1 g/kg).[63] How this translates into pregnancy and in particular how ideal body weight should be defined have not been studied.

Exposure to abnormal glucose levels during pregnancy, similar to that seen in nonsurgical women with GDM, warrants dietary intervention. In the case of hyperglycaemia, it is recommended to reduce rapidly absorbed carbohydrates, substituting them with protein and low glycaemic index (GI) alternatives (level 4).

Parenteral nutrition support may be indicated in cases of severe malnutrition during pregnancy[64] with initiation and choice of feeding route informed by local nutrition support protocols (level 4). In the absence of dietary advice specific to the postsurgery population, women should be encouraged to adhere to national guidelines regarding diet, taking into consideration changes of anatomy due to BS.

4.2 | Postprandial syndromes (dumping syndromes)

Postprandial syndrome, or dumping syndrome, is a common effect of bariatric and metabolic surgery. Postprandial syndrome (also termed early dumping syndrome) occurs within 60 minutes of ingestion of food, typically rapidly absorbed carbohydrates, producing symptoms including dizziness, flushing, and palpitations. If early dumping is suspected, rapidly absorbed carbohydrates should be avoided. Additionally, liquids should not be taken 30 minutes before and after eating to encourage a slower gastric transit (level 2−).[65,66] Caffeinated beverages should be avoided, and patients should be advised to eat slowly and chew well. Individualized advice relating to portion sizes and meal/snack frequency and spacing may be helpful alongside education about the GI of different foods (level 4).[66] Alcohol consumption can precipitate dumping and is in general contraindicated throughout pregnancy.[67]

Late dumping or postprandial hyperinsulinaemic hypoglycaemia (PHH) is far less common, although the exact prevalence remains unclear due to the lack of clear diagnostic criteria.[68-70] PHH characterized by symptomatic hypoglycaemia that occurs after 60 minutes of eating (typically between 60 and 180 minutes postprandial).[71] This syndrome should be considered in those who have symptoms of hypoglycaemia (eg, altered mental state, anxiety, sweating, or altered sensorium) that occur in parallel with biochemical evidence of hypoglycaemia, and which then resolve on ingestion of carbohydrate (ie, symptoms agree with Whipple's triad).[71]

In general, management of late dumping/PHH requires more careful dietary manipulation (ie, low GI carbohydrates, small carbohydrate portions, carbohydrates mixed with protein, frequent intake of six small meals) and sometimes referral to an endocrinologist for further investigation and medical management (level 4).[72] There is no specific approach for PPH described in pregnancy, although important glycaemic excursions potentially could affect fetal growth and well-being.

4.3 | Nutritional supplementation and monitoring

Men and women after BS have an increased risk to develop micronutrient deficiencies.[73] In the formulation of this guidance, it is recognized that there is a lack of evidence on the optimal nutritional monitoring and supplementation strategies in pregnancy after BS. We have therefore used data and guidelines for the nonpregnant postoperative population and supplemented this with pregnancy-specific data when available. It should be noted that we recommend that pregnancy should be planned and that nutritional supplementation should be optimized preferably 3 to 6 months prior to conception (level 4). A multivitamin and mineral supplement should be taken daily prior to conception and throughout pregnancy (level 4). This supplement should contain the following at a minimum: copper (2 mg), zinc (15 mg), selenium (50 μg), folic acid (5 mg), iron (45-60 mg or >18 mg after AGB), thiamine (>12 mg), vitamin E (15 mg), and beta-carotene (vitamin A, 5000 IU) (level 4). The retinol form of vitamin A should be avoided during pregnancy due to teratogenicity risk (level 2+),[74,75] and supplementation should be adjusted to maintain concentrations within normal limits (level 2−).[76]

Given the risk associated with potential deficiencies in the periconception period, the following indices should be checked at least every 3 months in women planning to become pregnant after BS: serum folate or red blood cell folate (level 2−),[77] serum vitamin B12 or transcobalamin (level 2−),[62,63,73,78,79] serum ferritin, iron studies (including transferrin saturation), full blood count (level 2−),[63,73,76,78,79] and serum vitamin A levels (level 2−).[76,80,81] In addition, the following should be monitored every 6 months: prothrombin time, international normalized ratio (INR) (level 2+),[82,83] serum 25-hydroxyvitamin D with calcium, phosphate, magnesium, and parathyroid hormone (PTH) (level 4), serum protein and albumin (level 2−),[62,78] renal function and liver function tests (level 4), serum vitamin E (level 4), serum zinc, copper, and selenium (level 4). Serum vitamin K1 concentration should be monitored if coagulation studies are abnormal (level 2+).[83]

Specific supplementation is recommended in the preconception and periconception period (Tables 3 and 4). In most patients after BS, 0.4 mg per day of folic acid is sufficient as doses >0.3 mg are not absorbed, due to lack of dihydrofolate reductase in intestinal cells. Despite having undergone BS, many patients still have a BMI > 30 kg/m^2. Current guidelines suggest that additional folic acid at a dose of 4 or 5 mg daily should be given to these patients during the periconception period and throughout the first trimester (level 4).[84] Postsurgery vitamin B12 regimens should be continued preconception at a dose of 1 mg every 3 months via intramuscular depot injection. Alternatively, oral supplementation (1 mg/day) can be used to increase compliance in the patient. However, a reduced absorption is to be expected as the secretion of intrinsic factor is diminished (level 4).[85] Additional vitamin B12 supplementation should be given as needed to maintain serum concentrations within normal limits (level 4). Iron supplementation should be continued at a minimum dose of 45 mg of elemental iron daily (>18 mg for AGB); this should be increased as needed to maintain ferritin within normal limits (level 4). Vitamin D should be supplemented to maintain a concentration of 50 nmol/L or greater with a serum PTH within normal limits (level 4). Calcium should be added to on-going vitamin D supplementation as needed to maintain PTH within normal limits (level 4). If vitamin K1 deficiency is measured or suggested by coagulation defects, it is advised to supplement this with an oral dose of 10 mg weekly (level 2+).[83]

During pregnancy, serum levels of many micronutrients and macronutrients will decrease as a result of the expanding maternal blood volume and increasing demands of the growing fetus. Therefore, it is recommended to check the following indices at least once per trimester and use pregnancy-specific ranges: serum folate (level 2−)[77]; serum vitamin B12 (level 2−)[62,63,73,78,79]; serum ferritin, iron studies including transferrin saturation and full blood count (level 2−)[63,73,76,78,79]; serum vitamin D with calcium, phosphate, magnesium, and PTH (level 4); serum vitamin A (level 2−)[76,80,81]; prothrombin time, INR, and serum

TABLE 4 Daily dose recommendations for (pre)pregnancy supplementation

Daily Dose Recommendations for (Pre)pregnancy Supplementation (Level 4)
Thiamine >12 mg
Folic acid 0.4 mg daily, during preconception and first trimester, 4-5 mg if obese or diabetic
Calcium 1200-1500 mg in divided doses (includes dietary intake)
Vitamin D >40 mcg (1000 IU)
Iron 45-60 mg elemental iron (AGB >18 mg)
Copper 2 mg (AGB >1 mg)
Zinc 8-15 mg per 1 mg copper
Vitamin K 90-120 μg
Vitamin E 15 mg
Vitamin A 5000 IU, should be in B carotene form in pregnancy
Selenium 50 μg daily

Abbreviations: IU, international units; AGB, adjustable gastric banding.

vitamin K1 concentration (level 2+)[82,83]; serum protein and albumin (level 2−)[62,78]; and renal function and liver function tests (level 4). In addition, we advise to monitor serum vitamin E, serum zinc, copper, and selenium (level 4) during the first trimester.

During pregnancy, thiamine 300 mg daily with vitamin B complex should be prescribed if prolonged vomiting occurs due to hyperemesis or other causes (level 3).[86-88]

Furthermore, intravenous thiamine should be given at a minimum dose of 100 mg daily with intravenous vitamin B complex if oral supplementation is not possible due to the severity of vomiting (level 3).[86-88] Further supplementation in regards to vitamin B12, iron, vitamin D, calcium, vitamin A, and vitamin K should be provided as in the preconception period (level 4).

Our recommendations for preconception nutritional supplementation generally agree with the British Obesity and Metabolic Surgery Society (BOMSS) and the American Society of Metabolic and Bariatric Surgeons (ASMBS) recommendations[63,84] and represent the commonly agreed standard of care with regards to micronutrient replacement.

4.4 | Breastfeeding

Limited data are available on breastfeeding after BS. In longitudinal studies, the composition of breastmilk from women after BS was found to be largely comparable with women without prior BS (level 2++).[89,90] Gimenes et al[91] found children born to mothers who had undergone BS and who were breastfed for at least 6 months to have lower fat mass and lower glucose levels, possibly protecting them from the development of obesity later in life. These authors therefore recommend breastfeeding in these women for at least 6 months in accordance to the general WHO guidelines (level 2+).[92] Case reports have demonstrated adverse maternal and/or neonatal outcomes due to micronutrient deficiencies during lactation (level 3).[93-95] Therefore, we advise supporting women wishing to breastfeed after BS (level 2+) and suggest that their nutritional status is closely monitored during lactation with additional supplements to those routinely advised after BS prescribed when necessary (level 3).

5 | ASSESSMENT AND PREVENTION OF MEDICAL COMPLICATIONS

5.1 | Ultrasound monitoring of fetal growth and anomalies

Most types of BS have been found to double the risk of fetal growth restriction (FGR) and SGA infants in comparison with BMI-matched women[96] and women with obesity.[97] This risk is higher with procedures that potentially further induce malabsorption (such as RYGB), when compared with procedures such as AGB or SG (level 2+).[96,98] Studies suggest that it would seem preferable for women of reproductive age to consider more restrictive procedures to limit this risk. AGB is however also associated with lower birth weight when the band remains inflated during pregnancy (level 2++).[99] Ultrasound monitoring of fetal growth should be offered to all women with a history of BS (level 2++). We recommend monthly screening from viability, especially in the presence of additional risk factors (eg, smokers, low GWG, teenagers) (level 4).

It is still unclear whether BS increases the risk for congenital malformations in the offspring as strong epidemiological data are lacking.[33] Several case reports and case studies have reported on the association between nutritional deficiencies in the mother and congenital anomalies in the offspring (level 3).[83,100-104] We therefore suggest an additional detailed anomaly scan during the late first or second trimester, especially in women with nutritional deficiencies (level 3), and sonographic follow-up of fetal growth during the third trimester (level 2++).

5.2 | Weight management in pregnancy

Weight regain following BS is a known problem in a substantial number of patients.[105-107] It is therefore important to avoid excessive GWG and postpartum weight retention in women after BS. On the other hand, insufficient GWG increases the risk for FGR and low birth weight.[108] So far, no specific guidelines for GWG during pregnancy in postbariatric women are available and few studies have focussed on the subject.

Overall, women with a history of BS gain less weight during pregnancy compared with women without prior BS, especially during the third trimester (level 2++).[27,109-113] Women who conceive within 18 months after surgery also appear to have less GWG in comparison with those who conceive after this period (level 2+).[27] Sheiner et al[114] compared GWG between different types of surgery and found a reduced GWG for vertical banded gastroplasty and silastic ring vertical gastroplasty when compared with RYGB, and higher GWG for AGB compared with all other forms of BS (level 2+).

Studies correlating GWG and pregnancy outcome are scarce. Ducarme et al[111] reported a significant reduction in both low birth weight (<10% centile) and macrosomia (>90% centile) after AGB compared with controls with obesity, despite lower mean GWG. In a small retrospective cohort, Santulli et al[115] reported no clear relation between birth weight and GWG in women after RYGB (level 2−). Stentebjerg et al[27] explored differences in outcome between women who gained appropriate, inadequate, or excessive weight according to the Institute of Medicine (IOM) guidelines for pregnant women.[116] GWG exceeding the guidelines increased the risk for preeclampsia and low Apgar scores at 1 minute (level 2+). Women with GWG below the guidelines delivered the smallest children. Lapolla et al[112] found a similar trend towards smaller children if GWG was below the guidelines. As pregnancy does not appear to affect long-term weight in women with a history of BS (level 2+)[25,26] and in view of the strong correlation between insufficient GWG, adverse neonatal outcomes, and increased risk of low birth weight in the general population, we advise women with a history of BS to adhere to the IOM guidelines (level 2+).

In women with AGB, evidence regarding band management and weight gain during pregnancy is also limited. Active band management appears to facilitate adherence to the IOM guidelines and was not associated with low birth weight (level 2++).[26,99,109,117] In contrast, band deflation was associated with macrosomia (level 3).[117]

We recommend health professionals caring for women after BS to measure BMI and monitor GWG in order to advise regarding adequate GWG relating to their prepregnancy BMI in accordance to the IOM guidelines (level 2+). If GWG is excessive, women should be assessed for complications (level 2+). In the case of insufficient GWG, diet should be revised and fetal growth carefully monitored (level 4).

5.3 | Diabetes screening

Currently, there are no specific guidelines on screening and treatment for diabetes during pregnancy in women after BS. The risk of developing type 2 diabetes (T2DM) and GDM is reduced in women after BS when compared with women without BS matched for their preoperative BMI.[118] In contrast, women who have undergone BS are often still affected by obesity or overweight and remain at higher risk for T2DM and GDM than women with a healthy weight without BS.[96,119] Undiagnosed diabetes in pregnancy results in an increased risk for adverse outcomes including fetal anomalies.[120]

Women who are planning to become pregnant post-BS should be screened for preexisting diabetes in the prepregnancy period, so that it can be identified and treated prior to conception (level 4). During pregnancy, women with a history of BS should routinely be screened for GDM (level 4).[121,122] Patients with other risk factors for developing GDM should be offered early screening according to local policies to exclude preexisting diabetes. This is best performed using fasting plasma glucose (FPG) or Hba1c (level 4). As data on cut-off values during pregnancies after bariatric surgery are lacking, we recommended using the guideline from the American Diabetes Association (ADA).[123] As such, the diagnosis of T2DM is made if HbA1c and/or FPG is greater than or equal to 6.5% and greater than or equal to 7.0 mmol/L, respectively. Care should be taken when using HbA1c as it is less sensitive to screen for T2DM and GDM using this method when compared with FPG. In addition, the HAPO study showed that associations with adverse outcomes were significantly stronger with glucose measures than with Hba1c.[124] However, this is offset by the test's greater practicality as it can be used in the nonfasting state, and the wider application of a more convenient test may increase the number of diagnoses made.

Oral glucose tolerance testing (OGTT) is appropriate for women with AGB and can be used to screen for GDM between 24 and 28 weeks (level 4).[122] However, given the physiological changes associated with RYGB, SG, and BPD, there are valid concerns with regards to the tolerability (dumping) and accuracy of OGTT in these women (level 2−).[121,122,125] Studies have suggested that using either a seven-point capillary blood glucose (CBG) profile or continuous glucose monitoring (CGM) or for 1 week between 24 and 28 weeks is the most appropriate method for GDM screening in these women (level 4). However, appropriate threshold values for random capillary glucose thresholds need yet to be defined in the post-BS population.

In the absence of specific outcome data for the post-BS population, it seems reasonable to aim for the same targets as used in the general population with GDM according to NICE[126] or according to local policies, that is maintaining capillary blood glucose concentrations below 5.3 mmol/L fasting, 7.8 mmol/L 1 hour after eating, and 6.4 mmol/L 2 hours after eating, if these goals can be achieved without hypoglycaemia (level 4). In women with a history of T2DM that is in remission postoperatively, additional value may be gained from screening with fasting glucose or HbA1c at booking and in the second trimester (level 4).[121] Screening in the third trimester should also be considered if there is a clinical suspicion of the interval development of diabetes (such as accelerated fetal growth indices).

If the diagnosis of GDM is made, it should be treated according to local policies (level 4). In general, this consists of lifestyle interventions first. If glycaemic targets are not met after 1 to 2 weeks, pharmacological treatment should be considered.[127]

5.4 | Mental health

BS is associated with an increased risk for mental health problems and substance abuse.[128-130] Data on mental health and substance abuse during pregnancies after BS are very limited. Higher anxiety rates during pregnancy are reported, without significant increase in depression rates (level 2+).[131] We found no data on postpartum depression following BS. Guelinckx et al[60] reported on maternal smoking during the first trimester of pregnancy in post-BS women. Overall smoking rate was 24%, without a clear relation to the type of procedure. Smoking prevalence was comparable with the general nonpregnant female population, but much higher than in the general pregnant population in the same region (6%). No studies were found reporting on alcohol or other substance abuse during pregnancies after BS. As such, we recommend health providers to screen for anxiety and other mental health disorders prior and during pregnancy, and follow-up should be offered when necessary (level 2+). Smoking cessation and alcohol use should be discussed when necessary as per general prepregnancy guidance (level 2−).

5.5 | Assessment and prevention of surgical complications

Evidence for two common surgical complications during pregnancy was found: internal herniation following RYGB and gastric band slippage following AGB. With regards to internal herniation, an incidence of 8% has been reported during pregnancies after RYGB.[132] Upper abdominal pain complicates 46% of such pregnancies, and internal herniation is diagnosed in 32.8% of these cases (level 3).[133] Women reporting abdominal pain had an increased risk of preterm birth and significantly lower birth weight compared with women without abdominal pain, suggesting that severe abdominal pain and abdominal surgery may induce uterine contractions (level 3).[133] Repeat internal herniation can occur in the same pregnancy even after previous closure of mesenteric defects (level 3). In a review of 22 cases of internal herniation during pregnancy after BS, all patients presented with abdominal pain and half of patients presented with nausea and/or vomiting. The most common location of the hernia was Petersen's space (45.5%), and there was a high incidence of maternal and fetal death in this case series (9% and 13.6%, respectively) (level 2−).[134] A systematic review reported that all maternal and perinatal deaths in pregnancies complicated by internal herniation after RYGB occurred in women treated later than 48 hours after symptom onset (level 2+ +).[135]

We recommend that all women with RYGB should be advised about the risks and symptoms of internal herniation and should seek appropriate medical assistance without delay. Care providers should be advised that any pregnant women with a history of RYGB that presents with abdominal pain should be assumed to have a small bowel obstruction due to internal herniation until proven otherwise (level 4)[136] and that imaging techniques and operative intervention, often performed with reluctance in pregnant women, should not be delayed (level 2++).

Gastric band slippage may be increased during pregnancy due to vomiting and increased intraabdominal pressure. One study reported an incidence of 12% during pregnancy compared with 3% to 5% in the general AGB population (level 3).[137] A shorter time interval between AGB and pregnancy was associated with a higher rate of primary band revisions after pregnancy (level 2+).[138] Patients should be

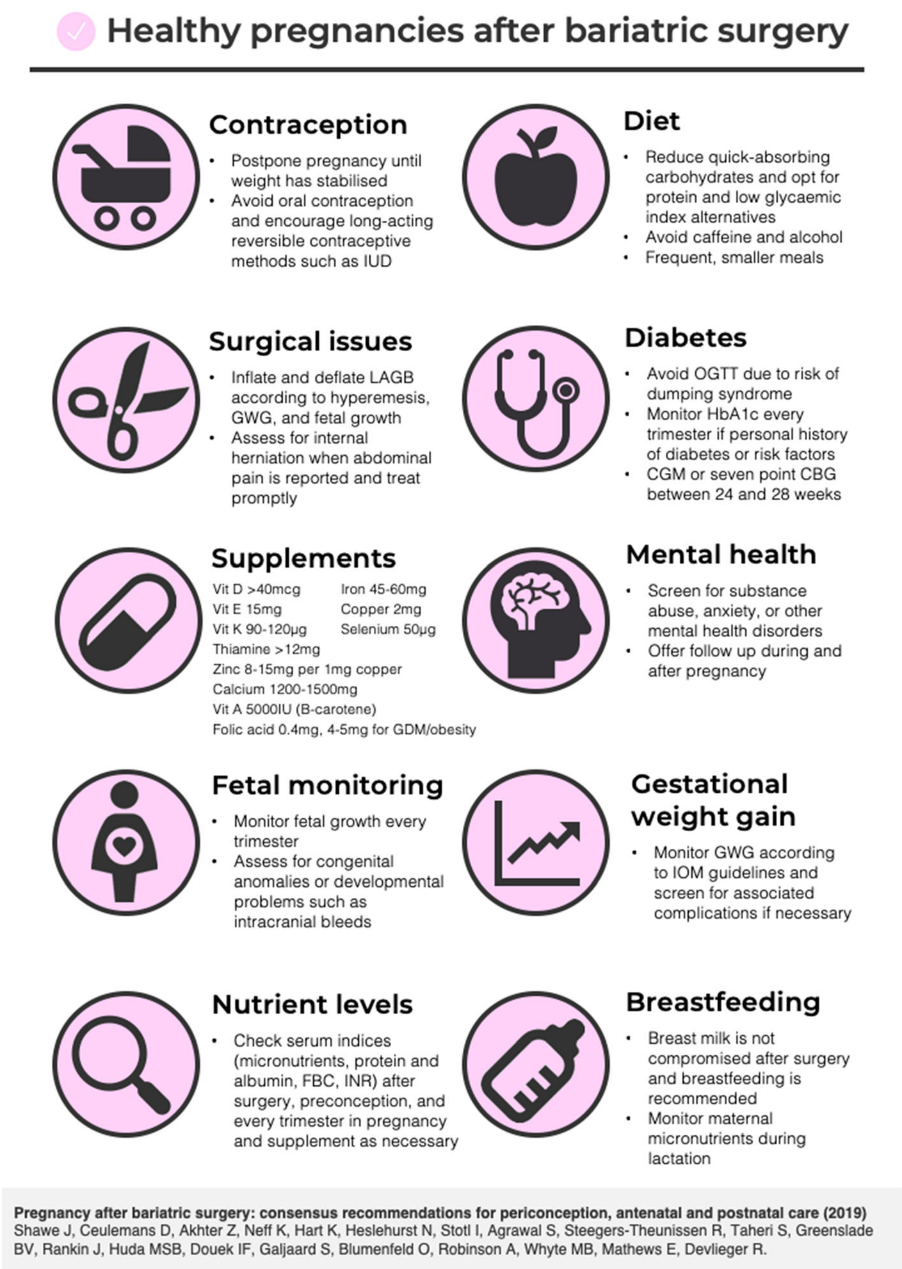

FIGURE 1 Print-friendly presentation of the recommendations for healthy pregnancies after bariatric surgery. [Colour figure can be viewed at wileyonlinelibrary.com]

counselled on the risk and symptoms of band slip during pregnancy and in the postpartum period (level 4).

5.6 | Research gaps

The recommendations issued in this review are based on a systematic research of the literature by a multidisciplinary group of international experts. The group has identified areas for which the level of evidence and therefore the quality of the recommendations is largely based on expert opinion. It is felt by the group that following areas need further robust investigation with regard to women and children's health in pregnancy following BS:

- Contraceptive counselling, safety, efficacy, and use
- Timing of pregnancy
- Gestational weight gain recommendations
- Nutrition during pregnancy
- Optimal macronutrient monitoring and substitution/supplementation such as protein intake, including management of supplementation and when parental nutrition should be considered
- Optimal micronutrient monitoring and substitution
- Prevention and treatment of dumping and PPH
- Monitoring of fetal growth
- Screening and treatment for GDM
- Screening and treatment of surgical complications
- Mental health and substance abuse

6 | CONCLUSIONS

This review summarizes current recommendations on the periconception, antenatal, and postnatal care of women following BS. Recommendations on the care of these patients are summarized in Table 3 and presented in a print-friendly format for practical use in the clinical setting (Figure 1). Our work highlights the paucity of studies on the optimal care for this growing group of women and identifies research gaps in this field. The publication of these guidelines will be the first step in a research collaboration which will address these unanswered questions.

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CONFLICT OF INTEREST

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Review Article

Management of Pregnant Women after Bariatric Surgery

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The prevalence of obesity is growing worldwide, and strategies to overcome this epidemic need to be developed urgently. Bariatric surgery is a very effective treatment option to reduce excess weight and often performed in women of reproductive age. Weight loss influences fertility positively and can resolve hormonal imbalance. So far, guidelines suggest conceiving after losing maximum weight and thus recommend conception at least 12–24 months after surgery. As limited data of these suggestions exist, further evidence is urgently needed as well for weight gain in pregnancy. Oral glucose tolerance tests for the diagnosis of gestational diabetes mellitus (GDM) should not be performed after bariatric procedures due to potential hypoglycaemic adverse events and high variability of glucose levels after glucose load. This challenges the utility of the usual diagnostic criteria for GDM in accurate prediction of complications. Furthermore, recommendations on essential nutrient supplementation in pregnancy and lactation in women after bariatric surgery are scarce. In addition, nutritional deficiencies or daily intake recommendations in pregnant women after bariatric surgery are not well investigated. This review summarizes current evidence, proposes clinical recommendations in pregnant women after bariatric surgery, and highlights areas of lack of evidence and the resulting urgent need for more clinical investigations.

1. Introduction

Obesity is associated with higher rates of cardiometabolic comorbidities and mortality and is increasing worldwide since decades. Effective weight loss approaches are necessary to overcome the negative long-term effects of obesity. Among lifestyle and medical treatment, bariatric surgery is a commonly used method in severely obese patients, which was demonstrated to result in good weight loss outcome. Between 1998 and 2005, the numbers of bariatric surgeries have increased by 800% [1]. These surgeries are performed in about 80% in women and about half of them in women of reproductive age. A British Registry report indicates that 53% of surgeries are performed in women between 18 and 45 years of age, a significant underrepresentation of non-Caucasian women and one-third of women having menstrual dysfunction [2]. Pregnant women after bariatric surgery have to be controlled regularly by a specialized team with specialists of various fields familiar with the management after bariatric procedures. The special needs of these pregnant women are to be addressed individually [3]. Supplementation of vitamins, minerals, and trace elements after bariatric surgery as well as during pregnancy is essential to avoid deficiencies and further arising complications in mother and child. Data from the US suggest poor screening for any deficiency in less than half of the women, but higher rates in pregnancy [4]. According to a recent survey, high unawareness (<20%) regarding nutritional recommendations and control was found among obstetricians [3].

2. Methods

Peer-reviewed literature reporting about bariatric surgery and pregnancy was critically examined. Using Medical Subject Heading (MESH) search terms in the PubMed database restricted to humans only and no time limit gave a result of 298 relevant articles from 1986 up to April 2018. Terms used in the search were obesity, bariatric surgery, and pregnancy linked with Boolean search operators. All abstracts were searched for relevant information about topics around the management of pregnant women after bariatric surgery. Pertinent literature was carefully examined, and further hand search was carried out to identify additional literature of relevance from the reference lists. Forward and backward literature searches were performed for highly important articles only and for literature regarding nutritional recommendations, deficiencies, and supplementation in pregnant women after bariatric surgery. Additionally, the homepages and published materials/guidelines of relevant national and international health, obesity, diabetes, surgical, and nutrition associations were searched to find further relevant information. The high variability of all sources of information led to the decision to perform a descriptive synthesis approach of the final 110 articles cited in our review. Level of evidence and grade of recommendation were assigned with the help of existing comprehensive reviews [5, 6].

3. Results

3.1. Obesity and Fertility. Obese women planning to conceive have a lower likelihood to become pregnant compared to lean women [7]. This decrease in fertility is primarily based on menstrual irregularities or anovulation. Overweight and obesity are associated with menstrual irregularities in a cross-sectional study reporting 30–47% of overweight/obese women presenting with menstrual anomalies, which correlates with increasing BMI [8]. Dissatisfaction with their sexual life was reported in about 50% of severely obese female and male patients [9]. Next to these findings, a longer duration of menstrual cycles was observed [10]. This might be caused by increased circulatory androgen concentrations (testosterone, DHEA-S), which are raised due to decreased hepatic SHBG production. Hepatic SHBG production is negatively influenced by hyperinsulinemia, which is more prevalent in obesity [10, 11]. Additionally, hyperinsulinemia triggers LH-mediated androgen production in ovarian theca cells [12]. These factors and their pleiotropic effects on other hormones cause an imbalance resulting in infertility. After weight loss surgery, a steep increase of SHBG and decline of testosterone, androstenedione, and DHEA-S levels were observed in obese women, which might help to overcome menstrual anomalies and infertility [13]. The quality of sexual life improves significantly over time in men and women after weight loss surgery due to significant increases in body image satisfaction [14].

3.2. Fertility after Bariatric Surgery. Clear decreases after bariatric surgery in prevalence of T2DM, PCOS, and menstrual irregularities were observed. Effects of bariatric surgery on fertility are mostly reported in small studies including small number of participants. Thus, evidence is limited and further studies are necessary to assess the effects of bariatric surgery on fertility and hormonal parameters. Reviews [1, 15] show a positive effect of weight loss through bariatric surgery on hormonal parameters with significant decreases in estrogen and testosterone and increases in FSH, LH, and SHBG. Furthermore, a decrease in TSH levels was observed, with no changes in free T4, increases in free cortisol, and decreases in cortisol binding protein [15]. Females after bariatric surgery reported normalization of menstrual cycles, regular ovulation, and more often spontaneous conception [1, 15]. A recent systematic review investigating gonadal dysfunction in obese patients and resolution of gonadal function after bariatric surgery found that 36% (95% CI 22–50) of women had PCOS. This resolved in 96% (95% CI 89–100) of women after surgical intervention with reduction of signs of hyperandrogenemia and amelioration of menstrual anomalies due to weight loss surgery [16].

3.3. Planned Pregnancy. Obese women in reproductive age aiming to perform bariatric surgery need to be informed that after bariatric surgery, the probability to get pregnant without sufficient contraception is increased. Rapid weight loss after bariatric surgery may reduce symptoms such as anovulation or cycle irregularities. Thus, in reproductive age, pregnancies are not recommended shortly after bariatric surgery and need to be planned after the phase of maximum weight loss, as short- and long-term consequences of rapid weight loss and potential micronutritional deficiencies on the offspring are not well investigated. At least 12 to 18 months and in some publications up to 24 months or until stabilization of weight after surgery are recommended between surgery and conception (evidence level 3, grade of recommendation D) [5–7, 17–19]. Individual progress of weight loss and weight stabilization needs to be addressed. When planning a pregnancy, regular control intervals with consultation of different specialities are recommended after bariatric surgery (Table 1). Limited evidence is available for conception before 12-month time lapse after surgery, but studies have shown comparable pregnancy outcomes comparing pregnant women before 12 months and thereafter [20]. Further studies demonstrated comparable rates of gestational diabetes mellitus, pregnancy-induced hypertension, birth weight, intrauterine growth restriction (IUGR), or small-for-gestational age (SGA) offspring [21]. However, little evidence exists about these aspects in women after bariatric surgery. After fasting in pregnancy ketonemia, increased urinary nitrogen excretion and decreased gluconeogenic amino acid production were reported, and due to

Table 1: Parameters and aspects recommended to control in women planning a pregnancy and during pregnancies after bariatric surgery.

History of preexisting comorbidities such as diabetes mellitus, retinopathy, nephropathy, neuropathy, or hypertension
Regular follow-up visits after bariatric surgery are recommended when planning a pregnancy:
(i) Nutritional counselling and monitoring of food intake, and exclusion of acute nutritional deficiencies
(ii) Half-yearly internal medicine and nutritional controls until two years postsurgical, thereafter 12-month intervals
(iii) Gynaecological/obstetric provision is strongly recommended
(iv) In case of nutritional deficiencies, controls have to be intensified, especially when pregnancy is planned
(v) Surgical controls if necessary or any complications occur (as well as recommended three months after surgery)
Pregnancy control interval:
(i) Obstetric examination at regular intervals at least every 4–6 weeks with control of weight, urine, and blood pressure, and narrower control intervals if complications occur, decided on individual basis
(ii) Regular fetal growth control (check for SGA and LGA) every 4–6 weeks starting from 24th week of pregnancy. Further Doppler ultrasound examinations might be necessary
(iii) Internal medicine and nutritional controls every trimester
(iv) Explore nutrient uptake, and check full blood count, clinical chemistry, coagulation, vitamins A, D, E, K, B12, iron status, folic acid, parathyroid hormone and protein, albumin, A1c, glucose, and TSH at least every trimester
(v) Additional laboratory controls if possible: thiamine and zinc
(vi) If necessary, closer intervals have to be considered on an individual basis (2–4 weeks in case of deficiencies, which need to be corrected).
Immediate contact with an experienced surgeon in case of unexpected symptoms (especially gastrointestinal)
Immediate consultation in case of emergencies:
(i) Acute persistent abdominal pain → consult: gynaecologist/obstetrician and surgeon
(ii) Persistent vomiting (consider thiamine deficiency; see below sections) → consult gynaecologist/obstetrician, internal specialist, and surgeon
A close interdisciplinary cooperation is highly necessary to provide optimal pregnancy outcomes
Specialized centres with experience in the care of pregnant women after bariatric surgery need to be contacted or should fully take care of pregnancies after bariatric surgery
Drugs not allowed in pregnancy should be discontinued before pregnancy if possible or switched to drugs allowed in pregnancy (e.g., ACE inhibitors, statins, several glucose-lowering drugs). If this is not possible, risk assessment has to be performed in agreement with the patient

physiological increases of insulin resistance in pregnancy, higher risk of ketonemia and ketonuria was suspected [22]. Thus, weight loss in pregnancy, especially shortly after bariatric procedures, might cause significant maternal metabolic changes, which potentially affect fetal development (growth, biometry, and malformation) or future disposition for healthy development and disease in offspring (neurocognitive, cardiovascular, and metabolic), which are underinvestigated so far.

If pregnancy occurs within time of maximum weight loss, short control intervals of mother and offspring are recommended with regular endocrine and metabolic examinations and documentation of general health appearance, weight curve, blood parameters, nutritional behaviour and nutritional intake, and advice (if necessary, sufficient supplementation with minerals, trace elements, and vitamins has to be prescribed; see below sections). Regular obstetric investigations monitoring fetal biometry with documentation of growth and well-being of the fetus, general health appearance of the mother, and planning of further pregnancy and birth modalities are necessary. If surgery-related complications cannot be ruled out, metabolic surgeons need to be involved early. It is recommended to plan delivery in a tertiary care centre with experienced interdisciplinary teams and the availability of a neonatal intensive care unit.

Women in reproductive age after bariatric surgery should be informed about the importance of nutritional supplementation in case of an emerging pregnancy and the need of compliance regarding intake and examinations. Pregnancy planning and waiting until time after maximum weight loss and optimization of nutritional supply (e.g., folic acid) before conception is favourable and should be recommended to all women undergoing bariatric surgery in reproductive age.

3.4. Contraception. A recent study reported that more than 4% of women tried to conceive in the first postsurgical year and another 41% had unprotected sexual intercourse during this time [23]. This study uncovers the need of more information about postsurgical contraception and time lapse between surgery and conception towards women after bariatric surgery. Oral contraception may not provide sufficient protection after bariatric surgery (especially in gastric bypass procedures). Malabsorption and complications such as vomiting and diarrhoea may cause limited effectiveness [19, 24]. There is lack of evidence due to low number of studies performed so far. A review summarizing five studies giving limited evidence concludes no reduction of effectiveness of oral contraceptives after bariatric surgery [25]. However, current ACOG guidelines recommend cautiousness, as in a few cases, pregnancies occurred unplanned. Lower absorption rates are suspected [19]. In particular, in RYGB and malabsorptive procedures, other contraceptive methods than oral ones are recommended (evidence level 3, grade of recommendation D) [5, 6, 19]. Undoubtedly, further evidence is urgently needed to increase knowledge about effectiveness of oral contraceptives after bariatric surgery.

3.5. Pregnancy. In case of pregnancy after bariatric procedures, follow-up visits and examinations have to be performed in short intervals (Table 1). If controls are missed or not scheduled, higher risk of persistent vomiting, gastrointestinal bleeding, anaemia, placental vascular disease, fetal neural tube defects, intrauterine growth retardation, or even miscarriage is reported [18]. In women with LABG, adaption might be necessary already starting from first trimester to prevent complications such as vomiting (evidence level 2, grade of recommendation B) [21, 26]. This so-called active gastric band management must be performed by an experienced surgeon.

Dietary advice and monitoring of food intake at regular intervals performed by trained dieticians with special knowledge of needs after bariatric procedures and experience in advising pregnant women are needed (evidence level 1, grade of recommendation A) [6, 19]. If possible, appointments should be performed before a pregnancy and at least every trimester in pregnancy and if necessary even at closer intervals (Table 1).

3.6. Examinations in Pregnancy. Pregnant women after bariatric surgery need to undergo regular examinations at least every trimester at specialized facilities (evidence level 3, grade of recommendation C) [5, 6, 19]. It is important to check nutritional state and recognize nutritional deficiencies at an early stage and try to prevent them [6]. Examinations also include blood sampling which should be performed at least once per trimester and include full blood count, clinical chemistry, coagulation, vitamins A, D, E, K, B12, iron status, folic acid, parathyroid hormone and protein, albumin, A1c, glucose, and TSH [6, 27]. According to Mechanik et al., several parameters have to be checked or ruled out which are included in Table 1 [6]. Table 1 provides further important aspects, which need to be considered.

3.7. Pregnancy and Obstetric Management. In general, bariatric procedures should not be regarded as a contraindication to deliver naturally [19, 28]. Nevertheless, increased rates of C-section in operated women are reported with some recent publications showing no differences [28]. However, huge variations in C-section rates were found in the literature ranging from about 18 to 60% section rate in operated women compared with 14–29% in control groups [28]. Explanations were found in a recent review, which discusses former C-section as the main issue, next to other aspects as maternal obesity, selection of the mother, the fetal position, and perceptions of treating clinicians [28].

3.8. Diagnosis of Gestational Diabetes Mellitus. Several studies have demonstrated that the prevalence of GDM decreases after bariatric procedures [29–31]. On the contrary, obese women have high risk of GDM throughout pregnancy: up to nearly 40%, with high incidences documented already in early pregnancy, and features of the MetSy, which might contribute to pregnancy complications [32, 33]. So far, the procedures that should be employed to diagnose gestational diabetes are unclear in pregnancies after bariatric surgery as several problems may arise. Depending on the type of bariatric surgery (e.g., RYGB), fast glucose absorption during an OGTT might lead to severe postabsortive hypoglycaemia [7]. Recent evidence demonstrates difficulties in the interpretation of OGTT results as plasma glucose concentrations after oral glucose load are altered following gastric bypass and characterized by rapidly changing glucose levels as well as high risk for reactive hypoglycaemic events following glucose load [34–37]. This might lead to misinterpretation of postprandial glucose levels as one-hour levels misleadingly appear too high, and two-hour levels appear too low, and thus, diagnostic alternatives to define impaired glucose tolerance in pregnancies affected by metabolic surgery need to be found. Moreover, testing of GDM might be related to serious adverse events as the dumping syndrome might occur especially in women after RYGB, omega loop, or sleeve gastrectomy [36]. Thus, no recommendations exist so far, which advise to perform an OGTT between 24 and 28 gestational weeks to diagnose gestational diabetes mellitus in women after bariatric surgery. As an alternative to an OGTT, ACOG [19] advised to perform home glucose monitoring for several days (i.e., about one week) with measurement of fasting and postprandial glucose levels and additional measurements if symptomatic (hyper- or hypoglycaemic event), which was also recommended by Adam et al. [36] between 24 and 28 weeks of gestation (evidence level 3, grade of recommendation D). Another alternative is to measure capillary glucose from 14 to 16 weeks of gestation with continuation throughout pregnancy [36]. Continuous glucose monitoring (CGM) or flash glucose monitoring (FGM) systems are an upcoming tool and of special interest as more and more easily implementable devices are available nowadays. These devices might be especially helpful in women with hypo- or hyperglycaemia at regular intervals and can help to evaluate glycaemic control. FGM was found to be safe and accurate in pregnant women with diabetes [38]. A recently published case report described the successful use of FGM in a pregnancy after RYGB complicated by GDM and nocturnal hypoglycaemia [39]. However, further studies are necessary to evaluate safety and accuracy of FGM in pregnant women after bariatric surgery. So far, alternative diagnostic methods have been described, but validated diagnostic criteria are not available. Diagnostic criteria to determine GDM in pregnancies and overt diabetes in early pregnancy following bariatric surgery are shown in Table 2 (evidence level 4, grade of recommendation D). Overt diabetes in early pregnancy is diagnosed as recommended for nonpregnant individuals after bariatric surgery [40]. In pregnancy, postprandial glucose levels are important for GDM diagnosis and treatment initiation as they are associated with fetal hyperinsulinemia, fetal growth, birth weight, and abdominal circumference. Due to changes in glucose absorption after bariatric procedures, rapid postprandial plasma glucose increases followed by rapid decreases and risk for dumping syndrome occur in many patients. In pregnant women after RYGB, postprandial hypoglycaemia was reported in nearly 55% up to 90% of

Table 2: Suggestions for diagnosis of gestational diabetes and overt diabetes in early pregnancy (<20 weeks of gestation) following metabolic surgery using capillary blood glucose monitoring (adapted from [40, 41]).

Fasting	≥95 mg/dl
1 h postprandially	In patients after gastric bypass/bariatric surgery of unknown significance (see text)
2 h postprandially	≥120 mg/dl
Overt diabetes diagnosis	
Fasting	≥126 mg/dl
HbA1c	≥6.5%
Random	In patients after gastric bypass/bariatric surgery of unknown significance (see text)

HbA1c values are applicable after bariatric surgery. Hypoglycaemia can also occur more than two hours after meal intake.

women after a 75 g OGTT between 24 and 28 weeks of gestation [34, 37]. Furthermore, higher incidence of SGA offspring and associations of postprandial glucose nadir with fetal growth were reported [34, 37]. Thus, the use of elevated 1 h glucose values solely for diagnosis and initiation of insulin treatment is not advisable, and fasting and 2 h postprandial glucose values seem to be better and safer parameters to base upon diagnostic and treatment decisions (evidence level 4, grade of recommendation D). A similar constellation exists in the diagnosis of overt diabetes before 20 weeks of gestation, which should be based upon fasting values and HbA1c. If a dumping syndrome is suspected, additional postprandial measurements beyond the 2 h measurement are necessary and recommended. In case of a diagnosis of gestational diabetes mellitus or overt diabetes in pregnancy, the controls need to be intensified and individual therapeutic approaches need to be developed. Similar perinatal outcomes and glycaemic control are reported in women with GDM after bariatric surgery and women with GDM without surgery [7].

The management of early or late dumping syndrome, as well as other complications (e.g., diarrhoea, flatulence, constipation, dysphagia, vomiting, food intolerance, and dehydration), is explained in detail elsewhere [42, 43]. Shortly, in early dumping, the amount of food per portion needs to be reduced and split into at least six meals a day [42]. A delay of liquid intake of at least 30 minutes after the meal is recommended. Management of late dumping includes the avoidance of rapidly absorbable and refined carbohydrates [42]. A case report demonstrated the beneficial use of acarbose in pregnant women after RYGB with severe progressive hypoglycaemic events as other interventions were not successful [42]. A significant reduction of postprandial hypoglycaemic events and the birth of a healthy girl at term with normal development were reported.

3.9. Weight Gain in Pregnancy. Weight gain in pregnancy should follow IOM recommendations, which are shown in Table 3 as no other evidence regarding weight gain recommendations in bariatric pregnancies exist (evidence level 4, grade of recommendation D) [19, 44]. Data so far reported lower weight gain in pregnancy after bariatric surgery compared with nonoperated obese women matched for BMI [21]. In a recent small study including women after RYGB, a mean gestational weight gain of 3.8 ± 12 kg was found and no differences in gestational weight gain were found when comparing women who became pregnant before or after the first year after surgery [45]. If weight gain in pregnancy does not follow IOM recommendations, more intense control intervals based on individual need have to be considered. Time lapse between surgery and conception might affect gestational weight gain and postpartum weight loss [7]. Fetal growth needs to be monitored in narrow intervals. A recent systematic review provides information that weight gain below or above the IOM recommendations for the respective weight class was associated with adverse perinatal outcomes [46]. In women with weight gain below the IOM recommendations, higher risk for SGA and preterm birth was reported.

3.10. Outcome. In general, a higher risk in obese pregnant women is well known for gestational diabetes, hypertension, preeclampsia, miscarriage, caesarean section, and stillbirth. In postbariatric surgery pregnancies, decreased risk for maternal complications was reported with approximation to risks of normal-weight women and improved neonatal outcomes compared with obese women without intervention [1, 5, 7, 18, 47]. In pregnancy, lower risk of gestational diabetes mellitus, hypertension, preeclampsia, and miscarriage was detected in operated women compared with obese women [17, 21, 28, 47]. Lower rates of preterm birth were reported, but also conflicting data exist with some studies reporting higher rates of LGA or SGA infants [7, 21, 25, 28]. Most studies report no differences in prematurity rate and perinatal death [21]. Recent results from a Swedish study representing more than 625,000 singleton pregnancies corroborate these results and demonstrate lower risk for GDM (OR 1.9% versus 6.8%; 95% CI 0.13; 0.47; $p < 0.001$) and lower pregnancy duration (273.0 versus 277.5 days; 95% CI; −2.9; −6.0; $p < 0.001$) [29]. However, diagnostic criteria for GDM in this study remain problematic. GDM was diagnosed based on the results of a 75 g oral glucose tolerance test according to the standard national criteria: if fasting plasma glucose exceeded 7.0 mmol/l (126 mg/dl) or 2-hour plasma glucose exceeded 10.0 mmol/l (180 mg/dl) [29]. In case of high risk of hypoglycaemia, fasting glucose and preprandial and postprandial glucose values were used for diagnosis instead [29]. Lower risk for LGA births (OR 8.6% versus 22.4%; 95% CI 0.24–0.44; $p < 0.001$) and higher risk for SGA (OR 15.6% versus 7.6%; 95% CI 1.64–2.95; $p < 0.001$) but also potentially higher intrauterine and neonatal mortality risk (OR 2.39; 95% CI 0.98–5.85; $p = 0.06$) were reported [29]. An Israeli observational study found significant reduction in diabetes mellitus (OR 0.6; 95% CI 0.4–0.9; $p = 0.009$), hypertensive disorders (OR 0.4; 95% CI 0.3–0.6; $p < 0.001$), preeclampsia (OR 0.2; 95% CI 0.1–0.7; $p = 0.005$), anaemia (OR 0.7; 95% CI 0.5–0.9; $p = 0.014$), and fetal macrosomia (OR 0.5; 95% CI 0.2–0.9; $p = 0.033$) in women after bariatric

Table 3: Weight gain in pregnancy according to preconceptional BMI, adapted by IOM Guidelines 2009 [44].

BMI	BMI limit (kg/m^2) (WHO)	Recommended weight gain in pregnancy (kg)	Recommended weight gain per week (2nd and 3rd trimesters)
Underweight	<18.5	13–18	0.5
Normal weight	18.5–24.9	11–16	0.5
Overweight	25.0–29.9	7–11	0.3
Obesity	≥30.0	5–9	0.2

surgery [48]. This study found no significant differences in GDM risk, but diagnostic criteria were not reported. A French observational study found significantly lower weight gain in women after LABG compared to obese women (5.5 versus 7.1 kg; $p < 0.05$) and lower risk for GDM (0 versus 22.1%; $p < 0.05$), preeclampsia (0 versus 3.1%; $p < 0.05$), low birth weight (7.7 versus 10.6%; $p < 0.05$), fetal macrosomia (7.7 versus 14.6; $p < 0.05$), and caesarean section (15.3 versus 34.4, $p < 0.01$). No differences were found in other neonatal outcomes. Diagnostic criteria for GDM were not published either in this study [49]. An American study investigating women before and after bariatric surgery found lower GDM incidence (OR 0.23; 95% CI 0.15–0.36) and lower risk for caesarean section (OR 0.53; 95% CI 0.39–0.72) in women after bariatric procedures [30]. The ICD-9 code for GDM was used to define GDM in this study. A recently published meta-analysis reporting maternal and neonatal outcomes of 20 cohort studies and including about 2.8 million subjects matched for presurgery body mass index found lower maternal risk for GDM (OR 0.20; 95% CI 0.11–0.37; number needed to benefit (NNTB) 5), hypertension (OR 0.38; 95% CI 0.19–0.76; NNTB 11), hypertensive disorders (OR 0.38; 95% CI 0.27–0.53; NNTB 8), postpartum hemorrhage (OR 0.32; 95% CI 0.08–1.37; NNTB 21), and caesarean section (OR 0.50; 95% CI 0.38–0.67; NNTB 9) [50]. Diagnostic criteria of GDM were not specified in this meta-analysis. Furthermore, lower risk for LGA (OR 0.31; 95% CI 0.17–0.59; NNTB 6) and higher risk for SGA (OR 2.16; 95% CI 1.34–3.48; number needed to harm (NNTH) 21), IUGR (OR 2.16; 95% CI 1.34–3.48; NNTH 66), and preterm deliveries (OR 1.35 95% CI 1.02–1.79; NNTH 35) were reported. No differences in congenital malformations between obese women and women after bariatric surgery were reported [50]. However, further research is necessary to evaluate the risk of congenital malformation as case reports have reported increased risk of neural tube defects after gastric bypass surgery [51, 52].

Long-term outcomes revealed that offspring of women after biliopancreatic diversion had lower overweight and obesity risk reduced to population risk up to 18 years after birth and no increase in underweight, better insulin sensitivity, lipid metabolism and ghrelin levels, lower inflammatory parameters and leptin levels, and less hypertension compared to offspring of nonoperated women [53, 54]. However, age differences between groups (10 versus 16 years) need to be considered as a relevant confounder [53]. Interestingly, in a cohort of siblings born before and after biliopancreatic diversion of their mother, weight was comparable at ages 1 and 6, but significantly higher rates of overweight/obesity at the age of 12 years were detected in siblings born before bariatric surgery of the mother [55], while other studies do not report any differences after birth up to the age of ten years or preschool age [56, 57]. However, during pregnancy, positive associations were observed between differences in gestational weight gain and sibling's birth weight [57]. Significant differences in DNA methylation were found in 5698 genes between offspring of women before and after bariatric procedures [58]. Metabolic improvement found in offspring after surgical procedures was correlating with methylation patterns in genes involved in cardiometabolic pathways, which clearly demonstrates the effect of maternal treatment of obesity on cardiometabolic parameters of the offspring at both epigenetic and transcriptional levels [58]. However, a case-control study investigating micronutrient deficiencies in 56 neonates of mothers with RYGB found higher rates of decreased cord blood levels below the 2.5 percentile for calcium, zinc, iron, and vitamin A and above the 97.5 percentile for magnesium, vitamin E, D, and B12 in RYGB offspring [59]. In a follow-up of offspring with a mean age of 46 months of women with gastric bypass, inadequate fibre intake in all children and deficiencies in calcium, vitamin A, and folic acid were found [60].

3.11. Abdominal Pain and Surgical Complications. During pregnancy after bariatric surgery, complications including intestinal obstructions or hernia, gastric ulcer, band, or staple line complications have been reported [21], which all need fast reaction to minimize maternal and fetal risks. Strong persistent abdominal pain, excess vomiting, and persistent nausea necessitate urgent consultation of an experienced metabolic surgeon (evidence level 3, grade of recommendation D). A Swedish cohort study identified significant higher risk of abdominal surgery in pregnancy [61]. Higher rates of laparotomies (1.5% versus 0.1%; OR 11.3; 95% CI 6.9–18.5) and higher rates of intestinal obstruction (1.5% versus 0.02%; OR 34.3; 95% CI 11.9–98.7) were reported. In case series, small intestinal obstructions or inner hernias in pregnancy were described [25]. In a case of persisting vomiting, intravenous supplementation of vitamins and/or trace elements together with fluid replacement needs to be considered. In particular, vitamin B1 (thiamine) deficiency needs to be considered as patients after RYGB and BPD-DS are at higher risk, and in pregnancy, hyperemesis gravidarum might aggravate this condition [62]. Symptoms of thiamine deficiency are Wernicke encephalopathy, oculomotor dysfunction, and gait ataxia. If Wernicke encephalopathy is suspected, the administration of intravenous solutions containing glucose may further deplete the remaining available thiamine and precipitate Korsakoff's syndrome [62]. In case of thiamine deficiency, intravenous thiamine infusion with 100 mg thiamine followed by consecutive intramuscular injection (100 mg/day for 5 days) and oral maintenance (50–100 mg/day) should be applied [62]. The application of oral antibiotics (recommended in pregnancy: amoxicillin for 7–10 days per month over two months) is recommended according to Lakhani et al. [63], who hypothesized small intestinal bacterial overgrowth due to alterations in gut microbiome following bariatric surgery as a cause for thiamine deficiency.

After insufficient long-term nutrient intake, the reinstitution of nutrient intake should be performed gradually and preferably in an inpatient setting under close monitoring of electrolytes including potassium and phosphorous, since a potentially life-threatening refeeding syndrome might occur. If a gastric band was implanted, a metabolic surgeon needs to assess a relaxation of the gastric band already in early pregnancy. In earlier studies, band migration with consequent complications (vomiting, disturbances in electrolyte and fluid balance, and band leakage) was described in nearly 29% [64]. A systematic review reported five neonatal and three maternal deaths and the necessity of acute surgical intervention in 20 cases in pregnancy with the majority of intervention due to internal hernia after RYGB [1]. Further, 23 women requiring urgent surgical intervention due to internal hernia but no death were reported in another study [65]. A recent case report describes acute bowel ischemia following thrombosis of the superior mesenteric artery in pregnant women after RYGB with loss of the fetus, several acute laparotomies, and subtotal enterectomy, preserving the first 20 cm of the jejunum [66].

3.12. Supplements during Pregnancy. Regular follow-ups to detect nutritional deficiencies before pregnancy and during pregnancy at least every trimester are recommended (Table 1). After bariatric surgery, micronutrient supplementation should be provided to all pregnant women (evidence level 3, grade of recommendation D). A recent systematic review summarizes several relevant cohort studies and case reports describing micronutritional deficiencies in pregnancies after bariatric surgery and found associations of vitamin K, A, B12, folate acid, and iron depletion with maternal and fetal complications (see sections below), but not for other micronutrients as calcium, zinc, magnesium, iodine, or copper [27]. The authors clearly concluded the need of further studies in this field as the information collected about subsequent adverse events concerning mother or child is weak and inconclusive [27]. The multicentre prospective cohort study AURORA will contribute to elucidate our knowledge about various aspects of women who underwent bariatric surgery including micronutrient deficiencies before, during, and after pregnancy [67].

3.12.1. Protein. According to German-Austrian-Swiss (D-A-CH) nutritional recommendations for normal pregnancy, daily protein intake is recommended with 0.9g protein per kilogram body weight in the second trimester and 1.0 g/kg in the third trimester [68]. Calculations are always based on normal weight (also in overweight/obese patients). During lactation, 1.2 g/kg is recommended [68]. Recommendations of daily intake for protein in pregnancy after bariatric surgery are not available and might depend on the type of bariatric surgery and time lapse from surgery.

3.12.2. Micronutrients

(1) Iron. Due to expansion of the blood volume, iron demand increases from 15 mg/d to 30 mg/d. Haemoglobin levels decrease physiologically. According to the WHO criteria, anaemia is defined as haemoglobin level below 110 g/l. The iron status should be examined at regular intervals, as well as haemoglobin levels, which determine the intensity of iron supplementation. Treatment of iron deficiency should start orally. Intravenous iron is not recommended in the first trimester [69]. Oral calcium and iron supplements interact and should not be taken in combination. Interestingly, in pregnancies with RYGB longer than four years time to conception, significantly lower haemoglobin levels (9.6 versus 11.1 g/dl; $p = 0.047$) and higher need of intravenous iron substitution or packed red cell transfusion were identified (30.8% versus 0%; $p = 0.026$) compared to women with less than 4 years time to conception [70]. Besides anaemia, no other significant complications in mother or child were reported [27].

(2) Calcium. Calcium homeostasis is strongly influenced by bariatric surgery as well as pregnancy. An acidic environment is required to allow absorption of calcium. Throughout pregnancy and lactation, a higher calcium demand is known, which may be critical for women after a bariatric procedure, regarding bone density and dental state [71]. Especially in the last trimester, a significant transfer from the mother to the fetus is observed to increase fetal skeletal mineralization. Thus, calcium is mobilized from the maternal calcium reservoir, which is mainly bone, and renal calcium retention, which increases risk for osteoporosis [71]. Higher calcium doses in pregnancies after bariatric surgery are recommended compared with normal pregnancies. Calcium deficiency was reported in 15.2% in the first and second trimesters and 20% in the third trimester in pregnant women after RYGB [72]. PTH excursions were found in 19.6, 30.4, and 32.6% from first to third trimester, respectively.

(3) Magnesium. Nocturnal calf cramps occur in 5–30% of pregnant women. They are associated with low magnesium levels. These can be well treated by oral magnesium supplements. In addition, it is useful in the prevention of muscular contractions of the uterus [73, 74]. High doses of magnesium can cause osmotic diarrhoea.

(4) Zinc. Low zinc levels, which also occur in pregnant women without bariatric surgery, are associated with early childbirth, low birth weight, and spina bifida. During lactation, eczema, dermatitis, and failure to thrive were reported in the offspring [75]. In order to prevent subsequent copper deficiency, at least 1 mg of copper should be given per each 8–15 mg of zinc substitution [43]. Zinc inadequacy in

Table 4: D-A-CH recommendations for supplementation of nutrients in pregnancies [68], tolerable upper intake levels according to EFSA [26] in pregnancy, and further nutritional recommendations in pregnancies after bariatric surgery according to Schultes et al. [25], Kaska et al. [75], Gonzalez et al. [28], Quyang et al. [7], Kushner et al. [62], ACOG [19], and Busetto et al. [5].

Nutrient	Recommended daily dietary intake during pregnancy (D-A-CH) [68]	UL (per day)	Pregnancy after bariatric surgery (per day)
Iron	30 mg	45 mg	100–200 mg [25], 40–65 mg [75], 65 mg [7], and 200 mg[8] [5]
Calcium	1000 mg[6]	2500 mg	1500 mg [25], 1000–2000 mg [75], 1200–1500 mg [28], 1200 mg [7], and 1000–1200 mg [5]
Vitamin D	20 μg = 800 IU[4]	100 μg = 4000 IU[4] [82]	400 IU [7], 1200–2000 IU [25], 2000–6000 IU [75], 1000 IU [5]
Vitamin A	1100 μg equivalent[1] from the 4th month	3000 μg = 10000 IU	No more than 5000 IU[1] [7, 75], 770 μg [28]
Vitamin E	13 mg equivalent[2,3]	300 mg, 1000 mg	—
Vitamin K	60 μg	—	120 μg [7]
Vitamin B12	3.5 μg	—	1000 μg every 3 months i.m. [5, 25], 350 μg orally/day or 1000 μg every month [75], 1000 μg/week i.m. or 350–500 μg/day p.o. [7]
Folic acid	550 μg	1 mg	600–800 μg [19], 400 μg [28], 800 μg [7], 4 mg [75], 400 μg or 5 mg[7] [5]
Iodine	230 μg	600 μg, 1100 μg	250 μg [75], 200 μg [28]
Zinc	10 mg	25 mg, 40 mg	11 mg [7], 20–30 mg [25], 15 mg [75]
Magnesium	310 mg	250 mg[5], 350 mg[5]	200–1000 mg [75]

UL = upper limit; IU = international unit. In general, most of vitamins and trace elements mentioned are contained in typically available supplements used in pregnancy (e.g., Femibion, Pregnavit). [1]1 mg retinol equivalent = 6 mg all-*trans*-β-carotene = 12 mg other provitamin A carotenoids = 1 mg retinol = 1.15 mg all-*trans*-retinyl acetate = 1.83 mg all-*trans*-retinyl palmitate; 1 IU = 0.3 μg retinol. [2]1 mg RRR-α-tocopherol equivalent = 1 mg RRR-α-tocopherol = 1.49 IU; 1 IE = 0.67 mg RRR-α-tocopherol = 1 mg all-rac-α-tocopheryl acetate. [3]1 mg RRR-α-tocopherol (D-α-tocopherol) equivalent = 1.1 mg RRR-α-tocopheryl acetate (D-α-tocopheryl acetate) = 2 mg RRR-β-tocopherol (D-β-tocopherol) = 4 mg RRR-γ-tocopherol (D-γ-tocopherol) = 100 mg RRR-δ-tocopherol (D-δ-tocopherol) = 3.3 mg RRR-α-tocotrienol (D-α-tocotrienol) = 1.49 mg all-rac-α-tocopheryl acetate (D, L-α-tocopheryl acetate). [4]1 μg vitamin D = 40 IU. [5]This UL does not include nutritional intake of magnesium from food or fluids and accounts for supplements only. [6]1200 mg calcium in women <19 years of age. [7]5 mg in patients with T2DM or BMI > 30 kg/m^2 until 12 weeks of gestation. [8]2–3 times daily. All NIH recommendations for women >18 years of age; i.m., intramuscular; p.o., per os.

pregnant women after RYGB was reported in 20%, with no associations to birth weight or maternal anthropometry [76].

(5) Iodine. Iodine deficiency is common in Middle Europe, and a recent analysis demonstrates iodine deficiency even in normal pregnancies [77]. Only 13.8% of the participating women were in the recommended range of 150–249 μg/l iodine urinary concentration despite commercially available iodized table salt. The upper urinary concentration of 250 μg should not be exceeded because of the significant association with subclinical hypothyroidism, whereas the WHO recommends not to exceed a urinary iodine concentration of 500 μg in pregnant women [78]. After bariatric surgery, limited resorption in women planning to become pregnant or in pregnant women might be associated with lower urinary iodine concentrations. Especially after malabsorptive interventions, evidence is scarce, particularly considering resorption of iodine happens in the stomach and small intestine. In nonpregnant subjects after malabsorptive interventions, increased urinary iodine concentration was found 3 to 18 months after bariatric surgery [79, 80] Furthermore, no iodine deficiency was identified ten years after gastric bypass or vertical banded gastroplasty [81]. So far, no studies reported maternal or fetal adverse events in pregnancy due to iron, calcium, magnesium, zinc, or iodine deficiency after bariatric procedures [27].

3.12.3. Vitamins. In general, substitution using vitamin supplements is recommended in pregnancy as well as after bariatric surgery, especially in case of deficiencies identified (evidence level 3, grade of recommendation D). Multivitamin preparations also for use in pregnancy may contain vitamin A or retinol equivalents and have to be prescribed cautiously because of potential teratogenicity in high doses. Table 4 shows nutritional intake recommendations in pregnancy.

(1) Vitamin D. In healthy adults, a daily vitamin D intake of 800 IU is recommended following D-A-CH recommendations [68]. The target level is a 25(OH)D serum concentration of above 50 nmol/l (20 ng/mL). The Endocrine Society recommends a maximal dose of 4000 IU/d in pregnancy or when planning to get pregnant [83]. In postbariatric populations, doses up to 6000 IU/d are discussed for nonpregnant women [6]. A study evaluating vitamin D status and its relations with ionic calcium and parathyroid hormone (PTH) in pregnant women after RYGB found vitamin D deficiency (≤20 ng/mL) or

insufficiency (>20–30 ng/mL) above 70% in all trimesters [72]. Negative correlations between calcium and PTH as well as an association of vitamin D with higher risk of urinary tract infection were reported.

(2) Folic Acid. Women planning to become pregnant should substitute folic acid after stabilization of their body weight. The substitution should start at least four weeks before conception and continue in pregnancy. There is no evidence on higher demands of folic acid in women after bariatric surgery [19]. A daily intake of 0.4 mg folic acid is recommended. Prevalence of folic acid deficiency was reported in 0–16% of pregnant women with bariatric procedures [84, 85]. Deficiencies of folic acid in and before pregnancy are associated with higher risk of neural tube defects. In a case series of three patients with no preconceptional nutritional counselling and poor postsurgical surveillance, severe neural tube anomalies were reported [86]. Thus, higher doses of folic acid up to 5 mg might be needed due to higher demands and deficiencies reported after bariatric surgery, which are also recommended in women with type 2 diabetes mellitus and body mass index above 30 kg/m^2 until twelve weeks of gestation [5].

(3) Vitamin B12. Vitamin B12 levels should be regularly controlled. In case of deficiency, vitamin B12 should be administered parenterally or orally if locally available. Prevalence of vitamin B12 deficiency was reported in about 50% of pregnant women with bariatric procedures [84, 85]. Neonatal vitamin B12 deficiency may cause irreversible neurologic defects and thus needs to be detected early [27, 87].

(4) Vitamin A. In the literature, recommended vitamin A doses are divergent. During pregnancy, the D-A-CH society recommends a retinol equivalent of 1100 μg (i.e., 3666 IU) per day from the fourth month of gestation onwards until the end of pregnancy. An upper limit of 5000 IU (1600 μg retinol equivalent) with inclusion of different vitamin A isoforms (retinol, retinol ester, β-carotene) in nutrition is described in American literature to prevent malformations [19, 75, 88]. The EFSA (European Food Safety Agency) stated in their most recent recommendation a tolerable upper intake level of 3000 μg/d retinol equivalent in pregnancy [89]. In women planning a pregnancy or pregnant women, the β-carotene form of vitamin A is recommended over retinol [43]. More than half of pregnant women with bariatric surgery were found to be deficient in vitamin A levels [84]. This was corroborated by two Brazilian studies evaluating vitamin A status among pregnant women after RYGB, which found inadequate serum retinol or β-carotene concentrations in about 60% of women during and after pregnancy with higher rates of symptoms (night blindness) reported (57% during pregnancy) [76, 90]. Significant associations of vitamin A deficiency with urinary tract infection and dumping syndrome were found. A case of severe maternal vitamin A deficiency after biliopancreatic diversion with premature birth and ophthalmologic and renal malformations was reported [91].

(5) Vitamin E. The elimination of free radicals is associated with vitamin E. The D-A-CH society recommends a daily intake of 13 mg tocopherol equivalent (=19.4 IU) [21], and the EFSA recommends a daily intake of 11 mg for women with no additional need in pregnant or lactating women and a 300 mg/d (=447 IU) upper tolerable intake level [92].

(6) Vitamin K. The D-A-CH society recommends a daily vitamin K intake of 60 μg. Due to lack of evidence, the EFSA could not define a tolerable upper intake level for vitamin K [93]. A daily intake of 70 μg phylloquinone is recommended [93]. After bariatric surgery, vitamin K shows reduced absorption and consequently transfers across the placenta. Thus, monitoring might be useful. Either direct measurement of vitamin K or indirect measurement of prothrombin time is possible. Deficiencies are reported in a high proportion of pregnant women after bariatric procedures reaching nearly 90% in first trimester and about half of the women at birth. In one study, no complications were reported [94]. However, five cases of intracranial bleeding associated with vitamin K deficiency and malformations have been described [95]. Furthermore, after biliopancreatic diversion, a case of vitamin K deficiency with maternal coagulopathy and vaginal hemorrhage and fetal hypocoagulability was reported [96]. These are rare but severe complications. Chronic complications including psychomotor and mental retardation from bleedings or even neonatal death were reported [27].

3.13. During Lactation. The lactational phase is a very important period for the development of the offspring. During lactation, regular examinations in 3-month intervals are recommended in women after bariatric surgery. In case of hyperglycaemia in pregnancy, fasting glucose or HbA1c control is advised four to twelve weeks after birth to document impaired glycaemic control postpartum. An oral glucose tolerance test should not be performed due to high risk of hypoglycaemic adverse events and high variability of glucose levels postprandially. Fasting glucose and HbA1c are recommended to be controlled and indicate a diagnosis of diabetes if they exceed 126 mg/dl or 6.5% (5.6 mmol) [40] (evidence level 4, grade of recommendation D). However, high variability of glucose levels was documented in postprandial glucose studied by continuous glucose monitoring (CGMS) [97]. Furthermore, CGMS detected high risk of postprandial hyperglycaemia in patients who were thought to have diabetes remission after surgery following actual guideline recommendations and had shown a normal fasting glucose and HbA1c [40, 97]. Thus, capillary home blood glucose monitoring with several time points postprandially, CGMS, or FGM may be offered additionally to collect fasting and postprandial glucose levels over a few days in case of uncertainty. Micronutrient deficiencies have to be identified with control of parameters as described above. Regular examinations of the newborn and examinations of the offspring in general are highly recommended.

The WHO recommends for all mothers to exclusively breastfeed until 6 months after birth. There are no exceptions

Table 5: D-A-CH recommendations of nutritional intake during lactation [68] and tolerable upper intake level (UL) according to EFSA Guidelines [102] or the NIH [103] for healthy nonbariatric women as well as recommendations for intake after bariatric surgery for women (when available, data specific for lactation are reported).

Nutrient	Recommended daily dietary intake during lactation (D-A-CH reference)	UL per day	Recommended daily intake after bariatric surgery
Iron	20 mg	45 mg	45–60 mg [6, 62] up to 300 mg [104]
Calcium	1000 mg[6]	2500 mg	1200–1500 mg [6, 62], 1500–2000 mg RYGB [104], BPS/DS 1800–2400 mg [62, 104]
Vitamin D	20 μg = 800 IU[4]	100 μg = 4000 IU[4] [82]	At least 3000 IU [6] up to 6000 IU [62]
Vitamin A	1500 μg equivalent[1]	3000 μg = 10000 IU	5000–10000 IU[9] [62, 104]
Vitamin E	17 mg equivalent[2,3,7]	300 mg, 1000 mg [62]	Lactation 19 mg, else 15 mg [62]
Vitamin K	60 μg	No recommendation	90–120 μg, BPS 300 μg [62]
Vitamin B12	4.0 μg[8]	No recommendation	1000 mg/month i.m. or s.c. [6, 62]. 350–500 μg p.o. [62, 104]
Folic acid	450 μg	1 mg	400 μg [6, 104], 400–800 μg, 800–1000 μg[10] [62]
Iodine	260 μg	600 μg, 1100 μg	—
Zinc	11 mg	25 mg, 40 mg	BPS 16–22 mg RYGB 8–22, mg, SG, LABG 8–11 mg [62]
Magnesium	390 mg	250 mg[5], 350 mg[5]	—

[1]1 mg retinol equivalent = 6 mg all-*trans*-β-carotene = 12 mg other provitamin A carotenoids = 1 mg retinol = 1.15 mg all-*trans*-retinyl acetate = 1.83 mg all-*trans*-retinyl palmitate; 1 IU = 0.3 μg retinol. [2]1 mg RRR-α-tocopherol equivalent = 1 mg RRR-α-tocopherol = 1.49 IU; 1 IU = 0.67 mg RRR-α-tocopherol = 1 mg all-rac-α-tocopheryl acetate. [3]1 mg RRR-α-tocopherol (D-α-tocopherol) equivalent = 1.1 mg RRR-α-tocopheryl acetate (D-α-tocopheryl acetate) = 2 mg RRR-β-tocopherol (D-β-tocopherol) = 4 mg RRR-γ-tocopherol (D-γ-tocopherol) = 100 mg RRR-δ-tocopherol (D-δ-tocopherol) = 3.3 mg RRR-α-tocotrienol (D-α-tocotrienol) = 1.49 mg all-rac-α-tocopheryl acetate (D, L-α-tocopheryl acetate). [4]1 μg vitamin D = 40 IU. [5]The UL does not include magnesium from nutritional sources or fluid and accounts for supplements only. [6]1200 mg calcium in women <19 years of age. [7]Around 260 μg RRR-α-tocopherol equivalent extra per 100 g secreted milk. [8]Around 0.13 μg vitamin B12 extra per 100 g secreted milk. [9]Depending on procedure, LABG 5000 IU, RYGB or SG 5000–10000 IU, BPS 10000 IU per day, β-carotene form does not contribute to vitamin A toxicity. [10]To women of childbearing age. All NIH recommendations for women >18 years of age; i.m., intramuscular; p.o., per os; BPS = biliopancreatic diversion; RYGB = Roux-en-Y gastric bypass; SG = sleeve gastrectomy; LAGB = laparoscopic gastric banding; DS = duodenal switch surgery.

known for mothers after bariatric surgery; however, concerns regarding micronutrient and vitamin deficiencies in exclusively breastfed offspring have been raised (evidence level 4, grade of recommendation D) [43]. Breastfeeding mothers need to be controlled and sufficiently supplemented because the maternal intake of nutrients has strong influence on the quality of the breast milk delivered to the offspring [98]. A recent study found significantly higher fat, energy, and a slightly higher carbohydrate breast milk content as well as no correlations between milk macronutrient composition and maternal diet in mothers after bariatric surgery compared with nonoperated controls [99]. Malnutrition of the mother can potentially cause undernourishment of the breastfed offspring. A sufficient vitamin and mineral supply is recommended. Especially vitamin B deficiency can cause megaloblastic anaemia and developmental delay in the offspring [43, 98, 100, 101]. Vitamin B12 deficiency in exclusively breastfed infants presenting with pancytopenia and long-term developmental delay was reported previously after RYGB caused by maternal vitamin B12 deficiency in breast milk [100, 101]. Calcium deficiency may lead to reduced calcium secretion in the breast milk and might cause undersupply and insufficient mineralization of the fetal bones [98]. However, evidence does not exist regarding supplementation of vitamins and trace elements after bariatric surgery during lactational period. The suggestions are derived from the D-A-CH guidelines for daily advised intake of nutrients in lactational period in women with no bariatric procedure as shown in Table 5 [68]. Furthermore, the upper intake levels and recommendations after bariatric surgery are shown.

4. Conclusions

The knowledge about the management of women after bariatric surgery in and around pregnancy is growing but consists mostly of data derived from retrospective studies or derived from few cohort studies and several case reports describing complications. However, there is little evidence in various important fields and aspects around pregnant women who underwent bariatric surgery with regard to ideal time of pregnancy after surgery, diagnostic criteria and best ways and methods to identify GDM, diabetes in pregnancy, and treatment goals after diagnosis. For pregnant women after metabolic surgery, further information on optimal weight gain in pregnancy, potential lack of several nutrients and nutritional intake recommendations in pregnancy and lactation, effects of nutritional deficiencies on fetal development, and long-term consequences in offspring is urgently needed and is of high scientific and clinical interest facing growing surgery numbers in women of reproductive age. These many uncertainties demonstrate a clear need of prospective studies focusing on filling these remaining gaps in knowledge. Based on the results and data collected in this review, further approaches and studies need to be conducted.

Pregnancies after bariatric surgery need to be considered as high-risk pregnancies with many potential complications, which may arise during pregnancy. These complications need to be accounted promptly to prevent acute or chronic complications in women with bariatric surgery or their offspring. Thus, care of these patients needs to be organized in an individual setting in a multilateral cooperation of various medical disciplines in specialized centres.

Disclosure

Alexandra Kautzky-Willer and Michael Krebs shared last authorship.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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Pregnancy after bariatric surgery – a narrative literature review

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Abstract

The purpose of this review was to analyze the literature about pregnancy after bariatric surgery. We searched for available articles on the subject from the last decade (2010 to 2020). The positive impact of bariatric surgery on the level of comorbidities and pregnancy and neonatal outcomes cannot be overrated. Weight loss after bariatric surgery reduces the incidence of obesity-related conditions in pregnancy. A pregnancy in a woman after bariatric surgery should be considered a high-risk pregnancy and taken care of by a multidisciplinary team with appropriate micronutrient and vitamin supplementation provided. Optimum time to conception should be chosen following the international recommendations. Every woman after bariatric surgery should be aware of symptoms of surgical complications and immediately contact their surgeon in case of abdominal pain.

Key words: *pregnancy, bariatric surgery, weight loss, intrauterine fetal growth retardation, gestational diabetes mellitus.*

Introduction

Obesity has become a global healthcare problem, with 13% of the world population (650 million) estimated to be obese in 2016 [1]. Bariatric surgery (BS) is known to be the most effective method of treatment, with the most durable weight loss and the greatest reduction of concomitant diseases [2, 3]. Women constitute the majority of patients undergoing bariatric treatment, most of them of reproductive age. Obesity is associated with many comorbidities, e.g. hypertension, diabetes mellitus and obstructive sleep apnea, but also influences fertility, the course of pregnancy and neonatal outcomes [4]. Obesity in pregnancy increases the risk of gestational diabetes mellitus (GDM), pregnancy-induced hypertension (PIH), prolonged labor, vacuum delivery, cesarean section, congenital anomalies and large for gestational age (LGA) infants [5]. Bariatric surgery reduces the risk of GDM, PIH, LGA, but also increases the risk of intrauterine growth retardation of the fetus (IUGR) and the proportion of small for gestational age (SGA) infants [6]. The alteration of the gastrointestinal absorption, hormone and metabolic changes may affect maternal and fetal well-being. Among the confirmed factors in the pathogenesis of impaired fetal growth are maternal micronutrient and vitamin deficiencies, but there are also other factors involved. The influence of BS on pregnancy and neonatal outcomes is subject to numerous studies. Pregnancy is associated with changes in body weight so that the influence of pregnancy and gestational weight gain on BS long-term outcomes remains an important question.

Aim

The aim of our review was to present recent studies about the relations between BS and pregnancy.

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We divided our review into sections presenting the problems we considered the most important: the influence of pregnancy on weight loss after BS, the incidence of surgical complications in pregnancy, the importance of time to conception interval, micronutrient and vitamin deficiencies, fetal growth impairment, pregnancy-induced hypertension, gestational diabetes mellitus and contraception.

Influence of pregnancy on weight loss after bariatric surgery

Most studies about BS and pregnancy are focused on the impact of BS on pregnancy and neonatal outcomes. The question about the influence of pregnancy on long-term results of BS is of utmost importance both for patients and bariatric surgeons. There is evidence that pregnancy does not have negative effects on the weight loss after BS. Weight loss after 5 years from the operation is comparable between patients who became pregnant after the operation and those who were not. The neutral effect of pregnancy on BS outcomes was confirmed in a recent study by Brönnimann *et al*., who compared the excess body mass index (BMI) loss after 5-year follow-up between women with and without a history of pregnancy and found it to be similar in both groups [7]. Quyên Pham *et al.* analyzed the history of weight loss of 84 women who became pregnant after BS and concluded that pregnancy after BS slowed down the pace of weight loss, but eventually did not affect weight loss after 5-year follow-up when compared to the control group of women without a history of pregnancy after BS [8]. Rottenstreich *et al.* conducted a cross-sectional case-control study that included 80 women who became pregnant after laparoscopic sleeve gastrectomy (LSG) matched with 80 controls for preoperative BMI, age and follow-up duration. After a follow-up of more than 5 years, they found no differences in long-term weight loss results [9]. Alatishe *et al.* conducted a study in a group of women after BS and did not find any differences in %EWL between those who became pregnant and those who did not [10]. Nevertheless, there are studies contradicting these results. Froylich *et al.* matched 62 patients after BS who were pregnant and had a delivery (before or after BS) with a control cohort of 92 patients after BS who had never conceived and found excess weight loss (%EWL) of 68.0% in the delivery group vs 53.0% in the group of subjects who had never conceived. They concluded that a pregnancy before BS resulted in reduced weight loss after BS [11].

Surgical complications during pregnancy

The most common complications after BS in pregnancy are internal herniation following RYGB and gastric band slippage following adjustable gastric banding (AGB) [5].

The incidence of internal herniation in pregnancies after a Roux-en-Y gastric bypass (RYGB) was reported to be about 8% [12]. The most frequent symptoms of internal herniation are upper abdominal pain, nausea and vomiting, which can easily be mistaken for early pregnancy symptoms [13]. Severe abdominal pain during pregnancy can increase the risk of uterine contractions, preterm delivery and SGA infants [14]. Previous closure of mesenteric defects does not exclude the possibility of internal herniation in pregnancy. In a review of 22 cases, the most common location of the hernia was Petersen's space [15]. Women after RYGB should be advised not to delay a consultation with a bariatric specialist in case of symptoms suggesting internal herniation as there are reports suggesting a higher incidence of maternal and fetal death in case of intervention after more than 48 h from the symptoms onset [16, 17]. Any pregnant woman after RYGB presenting with abdominal pain should be assessed for the possibility of diagnosis of internal hernia [13].

The risk of gastric band slippage is increased in pregnancy due to vomiting and higher intraabdominal pressure. Some reports suggest incidence of slippage of 12% compared to 3–5% to the general population after AGB [18, 19]. The symptoms of band slippage may also be mistaken for pregnancy symptoms [20].

Time to conception

International recommendations about pregnancy after BS (by Shawe *et al.* and the American College of Obstetricians and Gynecologists) agree that pregnancy should be postponed until the end of the rapid catabolic period of weight loss [5, 6]. The suggested interval between the surgery and conception differs between recommendations and ranges from 12 to 24 months. Pregnancies started before the end of the rapid catabolic period are at higher risk of miscarriage, fetal malnutrition and impaired growth

Table I. Recommended daily dosage of micronutrients and vitamins for (pre)pregnancy supplementation (after Shawe J *et al*. Pregnancy after bariatric surgery: consensus recommendations for periconception, antenatal and postnatal care. Obes Rev 2019; 20: 1507-22)

Micronutrient	Recommended daily dosage
Folic acid	0.4 mg (4–5 mg if obese or diabetic)
Calcium	1200–1500 mg (including dietary intake)
Vitamin D	> 40 µg (1000 IU)
Iron	45–60 mg (elemental iron)
Copper	2 mg
Zinc	8–15 mg per 1 mg copper
Thiamine	> 12 mg
Vitamin K	90–120 µg
Vitamin E	15 mg
Vitamin A	5000 IU (as B carotene)
Selenium	50 µg

[5, 6, 21]. Some authors emphasize the need of a patient-centered approach in assessing the optimum time for conception. Mahawar *et al.* suggested that instead of imposing a fixed time interval after the operation, it would be better to advise conceiving after at least 2 months of stable weight after the weight loss period [22]. Some studies suggest that a time to birth interval of less than 2 years was associated with a higher risk of preterm delivery, neonatal intensive care unit (NICU) admission and SGA infants [23].

Contrary to the international recommendations about the optimum time for pregnancy after bariatric surgery, there are studies showing no differences between pregnancy and neonatal outcomes if the time of conception followed the recommended time interval between BS and pregnancy. The analyzed endpoints were: preterm deliveries, birth weight, SGA neonates, NICU admissions, gestational weight gain (GWG), hyperemesis, nutritional deficiencies, GDM and PIH [24–27].

Pregnancy and nutritional deficiencies after bariatric surgery

BS, especially malabsorptive procedures, leads to various micronutrient and vitamin deficiencies due to changes in gastric pH, dumping syndrome and absorption changes [28]. There are international guidelines indicating the optimum dietary supplementation after BS and during pregnancy after BS; however, the problem remains in patients' adherence to the recommendations, which decreases with increasing time since surgery [5, 6]. The level of deficiencies rises with the decrease of patients' adherence to the recommendations. Maternal micronutrient and vitamin deficiencies may lead to impaired fetal growth [29, 30].

The recommended minimum protein intake during pregnancy is 60 g of protein a day, although it should be adjusted for the patient's BMI and lean body mass. Rapidly absorbed carbohydrates should be avoided due to the risk of early and late postprandial syndrome. Pregnancy should be planned with the help of a multidisciplinary team and a multivitamin and mineral supplement should be taken prior to and throughout pregnancy [5]. Some patients restrict the daily caloric intake against medical advice because of their fear of regaining weight, sometimes to a level that may negatively affect the fetal well-being and intrauterine growth. The role of dietitian nutritionists and psychologists in the multidisciplinary care of a pregnant woman after BS cannot be overvalued. The suggested daily supplementation in pregnancy is presented in Table I.

The most commonly diagnosed deficiency is maternal anemia, often diagnosed before pregnancy. The incidence and level of maternal anemia increases in pregnancy due to higher demand of the developing fetus [31–33]. The incidence of maternal anemia during pregnancy is higher after malabsorptive procedures [34, 35]. Coupaye *et al.* in a study including 123 pregnancies after BS found a positive correlation between the risk of SGA infants and maternal protein intake and a negative correlation with the maternal iron status [36].

Rottenstreich *et al.* conducted a systematic review of 27 studies on maternal nutritional deficiencies in pregnancies after BS. The deficiencies found after both restrictive and malabsorptive procedures were iron, folate, vitamin B_1, B_{12} and D. Additionally, the researchers found that there was an increased risk of maternal anemia in positive correlation with the time to conception length [37]. The level of circulating vitamin K_1 is lower in pregnant patients after BS and supplementation is of utmost importance to prevent fetal and neonatal intracranial hemorrhages [38].

Low blood glucose levels, often diagnosed after RYGB and other types of bypass BS, can lead to impairment of fetal growth. As stated by Rottenstreich *et al.*, maternal hypoglycemia and subsequent fetal hypoglycemia are a common consequence of BS, especially malabsorptive surgery (MS). After the oral glucose tolerance test (OGTT), hypoglycemia was found in more than 50% of patients after BS and 83% of patients after MS [39]. Low inflow of glucose to the fetus may result in IUGR and SGA infants and maternal hypoglycemia may be present for a substantial portion of time in mothers after MS. OGTT is currently considered an unacceptable method of screening for GDM in women after all types of BS procedures except for AGB, which does not cause direct metabolic changes. Late postprandial syndrome and reactive hypoglycemia occurring after BS lead to lessened tolerance and accuracy of OGTT, excluding it as a method of diagnosing GDM in pregnant patients after BS. OGTT should be substituted with monitoring of capillary blood glucose levels between the 24th and 28th week of gestation or continuous glucose monitoring [5, 40–42].

Fetal growth impairment

The vast majority of studies show a decreased rate of GDM, PIH and LGA in pregnancies after BS and an increased risk of IUGR and SGA infants.

There is an important question whether all types of bariatric procedures lead to similar pregnancy and neonatal outcomes, or whether there are differences. LSG remains the most popular BS procedure in the world and its influence on pregnancy course has to be well established. The risk of SGA infants after MS has been confirmed in many studies [43]. One of the most important studies in the field was a national Swedish cohort study, which included 670 pregnancies after BS, 98% out of whom had a history of RYGB. The study presented a more than two-fold increase in risk of SGA neonates after BS (15.6 vs. 7.6%) [44]. Kjaer *et al.* presented an analysis of 339 pregnancies after BS; 84.4% after RYGB. The risk of SGA infants was 2.3 times higher after BS than in the control group [45]. An increase in the risk of SGA neonates after RYGB was also found by Belcastro *et al.* [46].

There are also studies comparing purely restrictive procedures, such as laparoscopic adjustable gastric banding (LAGB) with MS. Chevrot *et al.* found a two-fold increase of the risk of SGA infants after RYGB, compared to LAGB and in the general population [47]. In a study by Facchiano *et al.* the mean birth weight of neonates was lower after RYGB than LAGB [48]. A meta-analysis of 33 studies by Akhter *et al.* did not find any correlation between incidence of SGA infants and restrictive surgery (RS), contrary to an increased risk after MS [43]. A study by Aricha-Tamir *et al.*, who analyzed paired pregnancies before and after BS, found no association between BS and the risk of SGA infants [49].

Some studies present a comparable risk of IUGR and SGA neonates after RS and MS [50]. Coupaye *et al.* found in their study, in which they included 123 pregnancies after BS (77 after RYGB and 46 after SG) a comparable rate of IUGR and SGA infants between both types of procedures [36]. No differences in the risk of SGA neonates between pregnancies after RS and BS were also found by Sheiner *et al.* and the risk of IUGR was 2.5 times higher after BS compared to the control group [51]. The importance of the risk of SGA infants after LSG was analyzed by Rottenstreich *et al.* in a recent case-control study that included 119 pregnancies after LSG compared to obese controls. They found a more than three-fold increase in the incidence of SGA infants after LSG (4.3 vs. 14.3%), having confirmed an increased risk of SGA infants after RS [52]. These findings suggest that there are more mechanisms involved in the pathogenesis of growth restriction after BS, not only the absorption changes.

Pregnancy-induced hypertension and pre-eclampsia

Pregnancy-induced hypertension is defined as de novo onset of hypertension diagnosed after the 20th week of gestation, with > 140 mm Hg systolic or > 90 mm Hg diastolic. Preeclampsia is a multi-systemic disease with at least one new-onset condition complicating the course of PIH, including proteinuria and other maternal organ dysfunction: renal insufficiency, liver involvement, neurological and hematological complications. Both PIH and preeclampsia can negatively affect the pregnancy course, leading to adverse pregnancy and neonatal outcomes, including preterm delivery and IUGR. Preeclampsia remains the leading cause of maternal and neonatal morbidity and mortality worldwide [53]. The pathogenesis of preeclampsia starts with abnormalities in placenta development, angiogenesis alterations and abnormal trophoblastic invasion [54, 55]. Obesity-related metabolic factors may influence the cytotrophoblast and endothelial dysfunction, increasing the risk of preeclampsia [56]. Obesity is a major risk factor of developing preeclampsia, with a strong positive association between pre-pregnancy BMI and the risk of preeclampsia, doubling with each 5–7 kg/m^2 increase in pre-pregnancy BMI [57]. The risk of preeclampsia is three-fold higher in obese women compared to the general population [31]. Reducing GWG in obese patients decreases the risk of preeclampsia, but increases the incidence of SGA infants [58]. Most studies show that BS is associated with a significant reduction of risk of preeclampsia. A meta-analysis by Galazis *et al.* based on 17 cohort and case-control studies showed a lower incidence of preeclampsia after BS with an OR of 0.45 [59]. Bennett *et al.* analyzed 269 pregnancies before and 316 after BS and found a substantial reduction of incidence of preeclampsia (OR = 0.20) and PIH (OR = 0.16) [60]. The reduction of incidence of PIH and preeclampsia in patients after BS has been confirmed in numerous studies and meta-analyses [30, 31, 61–65].

Gestational diabetes mellitus

Obesity is a well-known risk factor for developing diabetes mellitus, the incidence of which can be significantly reduced after bariatric surgery [66, 67]. Gestational diabetes mellitus is a condition of abnormal maternal glucose tolerance that is diagnosed for the first time during pregnancy. High pre-pregnancy BMI is a risk factor for GDM and developing type 2 diabetes mellitus after pregnancy [68]. GDM can lead to disturbances in fetal development, including fetal macrosomia and a four to five times higher rate of congenital malformations than in the non-diabetic population [69]. BS and the following reduction of body weight leads to an important decrease in the rate of GDM, when compared to the obese population, and in some studies even to the general non-obese population. The vast majority of studies on the influence of BS on the pregnancy course confirm a significant reduction in the incidence of GDM after BS [30, 42, 70, 71]. Johansson *et al.* found a more than three-fold reduction of the incidence of GDM in patients after BS compared to the obese population, and the results were corroborated in an analysis by Burke *et al.* [44, 72]. In one of our studies we observed a two-fold decrease in the proportion of GDM in patients after BS compared to the general non-obese population [34]. A meta-analysis by Galazis *et al.* based on 17 studies also demonstrated a two-fold decrease in incidence of GDM [59]. The decrease in incidence of GDM has been confirmed in other studies [19, 49, 73].

Contraception

Women after bariatric surgery are recommended to delay conception for the period of rapid weight loss of at least 12 to 24 months, and pre-operative counseling about appropriate and effective methods of birth control is of utmost importance. Mengesha *et al.* observed in their study that even a single counseling visit ameliorated the rate of optimum contraception use after BS [74].

According to the consensus recommendations by Shawe *et al.*, BS can impair the absorption of both estrogen and progestagen components of oral contraceptives and therefore combined oral contraception can be less effective after BS [5, 75]. However, studies confirming those statements are based on populations after older types of procedures, such as BPD, AGB or jejunoileal bypass [76–79]. There is no level 1 evidence confirming the compromised absorption of combined oral contraception, and some new studies suggest normal pharmacokinetics of etonogestrel after BS [80]. Further studies are necessary to evaluate the real risk of reduced efficacy of oral contraception after BS.

Additionally, oral contraception should be advised against in obese pre-operative patients and those still affected by obesity after BS due to increased risk of venous thromboembolism [81, 82]. Nevertheless, there are studies presenting the same proportion of oral contraception use before and after BS, sometimes even at the level of 15% of the population, which further emphasizes the importance of pre-operative counseling [83, 84].

Patients after BS should be advised to use long-acting reversible methods of contraception, such as intrauterine devices and progestagen implants, followed by non-hormonal barrier methods in women preferring those (male and female condoms may be suitable; diaphragms require adjustment of size after every 3 kg of weight change) [5, 85–88].

Conclusions

Bariatric surgery has a positive impact on pregnancy outcomes through reduction of obesity-related comorbidities. The proportion of gestational diabetes and preeclampsia in patients after BS is significantly decreased. However, there are also negative effects of BS on the pregnancy, such as a higher risk of IUGR and SGA infants, as well as maternal micronutrient and vitamin deficiencies. There is also a higher risk of surgical complications after BS, especially internal herniation after RYGB. A pregnancy in a woman after bariatric surgery should be considered a high-risk pregnancy, and a multidisciplinary team, including an experienced obstetrician, a bariatric surgeon, a dietitian nutritionist and a psychologist, should take care of every pregnant woman after weight loss surgery. Appropriate micronutrient and vitamin supplementation in accordance with current recommendations should be provided. An alternative form of screening for gestational diabetes mellitus has to be implemented. Optimum time to conception should be chosen following the guidelines, but also individually consulted in each case. Appropriate and efficient contraception should be introduced and birth control counseling should always be included in pre-operative care. Every woman after bariatric surgery should be aware of the symptoms of surgical complications and immediately contact their surgeon in case of abdominal pain.

Conflict of interest

The authors declare no conflict of interest.

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