Canadian Agency for Drugs and Technologies in Health

RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

TITLE: Obstetric, Neonatal, and Child Outcomes for Women with Previous Bariatric Surgery: A Review of the Clinical Evidence

DATE: 5 September 2014

CONTEXT AND POLICY ISSUES

Bariatric surgery is a term used to describe a number of elective surgical procedures that modify the gastrointestinal tract to either limit the volume of food a person can consume at one time (restrictive) or to restrict the nutrients that can be absorbed (malabsorption).[1] According to the Canadian Institute for Health Information (CIHI), in 2012/2013 close to 6,000 bariatric surgical procedures were performed in Canada.[1] This number represented an increase of more than 250% from 2006/2007.[1] In 2012/2013, 53% of bariatric surgeries were gastric bypass, 28% were sleeve gastrectomy, and 15% involved gastric banding (the remainder were made up of other procedures).[1] Eighty percent of bariatric procedures are performed on women and 65% of individuals undergoing surgery are less than 50 years of age.[1] Obesity is defined as a body mass index (BMI) greater than or equal to 30 kg/m^2 while the normal BMI range is considered to be 20 to 25 kg/m^2.[2,3]

The intention of bariatric surgery is to help individuals lose weight and, in turn, reduce the incidence of obesity-related complications such as type 2 diabetes mellitus, hypertension, and hernia.[1] Obesity-related complications can be of particular concern when women are attempting to become pregnant. Obesity may impact a woman's fertility or increase her risk of miscarriage.[4] Other obesity-related obstetric complications may include gestational diabetes mellitus, gestational hypertension, pre-eclampsia, post-partum hemorrhage, and babies that are large for their gestational age.[4]

As bariatric surgery is performed more frequently on women who are in their childbearing years, concern has emerged as to whether there are any negative consequences to the mother or child associated with pregnancy and childbirth following these procedures. While there may be benefits related to maternal weight loss before pregnancy, there are also questions as to whether malabsorptive procedures could lead to inadequate fetal nutrition and complications and whether pregnancy is safe for the mother following these procedures.[4]

The aim of this report is to examine the evidence and to identify the positive or negative impact on maternal, neonatal, and child outcomes resulting from pregnancies following bariatric procedures.

RESEARCH QUESTION

What is the clinical evidence regarding obstetric, neonatal, and child outcomes for women with previous bariatric surgery?

KEY FINDINGS

The results of the studies included in this review generally suggested that pregnancy after bariatric surgery, both restrictive and malabsorptive, was safe for mother and child. There were some positive effects observed on potential maternal and neonatal outcomes that could be attributed to decreased BMI. There was no evidence to indicate that there was an increased risk of congenital malformation for children born following bariatric surgery. The authors generally concluded that additional larger studies may be required before a definitive conclusion regarding safety can be made.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 7), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. The search was limited to English language documents published between January 1, 2009 and August 7, 2014.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria	
Population	Women who have had bariatric surgery then become pregnant
Intervention	Bariatric surgery: laparoscopic adjustable gastric banding, laparoscopic Roux-en-Y gastric bypass, laparoscopic sleeve gastrectomy
Comparator	Women who are pregnant and have not had bariatric surgery
Outcomes	Obstetric, neonatal and child outcomes (fetal growth, intrauterine growth restriction, fetal or maternal malnutrition, perinatal death, Apgar score, macrosomia, congenital abnormalities, child growth, child neurodevelopmental outcomes, pre-eclampsia, labour induction, caesarean section, post-partum hemorrhage, gestational diabetes, miscarriage, post-partum infection, hypertension, twins).
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and non-randomized studies

Exclusion Criteria

Studies were excluded if they did not satisfy the selection criteria, if they were duplicate publications, if they were included in the identified systematic reviews, or were published prior to January 1, 2009.

Critical Appraisal of Individual Studies

Key methodological aspects relevant to each study design were appraised and summarized narratively. The quality of systematic reviews was assessed using the AMSTAR checklist[5] and non-randomized studies were assessed using the Downs and Black instrument.[6] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 325 citations were identified in the literature search. Following screening of titles and abstracts, 303 citations were excluded and 22 potentially relevant reports from the electronic search were retrieved for full-text review. No additional potentially relevant publications were retrieved from the grey literature search. Of these potentially relevant articles, 11 publications were excluded for various reasons, while 11 publications met the inclusion criteria and were included in this report. Appendix 1 describes the PRISMA flowchart of the study selection.

Summary of Study Characteristics

Study Design

Two systematic reviews[2,3] and nine non-randomized studies[7-15] were identified regarding maternal and offspring outcomes following maternal bariatric surgery. One systematic review included 11 observational studies, four with and seven without control groups,[2] and the other included 17 studies but did not indicate which study types were included.[3] Studies included in the Kjaer review were published before 2012[3] and no date limits were indicated in the Vrebosch review.[2] All of the non-randomized studies examined retrospective cohorts of patients.[7-15]

Country of Origin

The systematic reviews were undertaken by groups based in Denmark[3] and Belgium.[2] One non-randomized study was conducted in Brazil,[9] two in Israel,[7,10] two in Denmark,[8,14] and four in Sweden.[11-13,15] None of the identified studies were conducted in North America.

Patient Population

All of the studies examined women who became pregnant after undergoing bariatric surgery for weight loss.[2,3,7-15] These pregnancies were compared with the same woman's own pregnancy before undergoing bariatric surgery[7,9,11,12] or other normal weight[2,3,8,13-15] or obese[2,3,8,10,13-15] women who were pregnant and had not undergone bariatric surgery.

Interventions and Comparators

One of the systematic reviews[3] and the majority of the included studies[7,9-15] examined the outcomes of pregnancy following any bariatric surgery (either restrictive or malabsorptive). One systematic review limited the intervention to only restrictive laparoscopic adjustable gastric banding (LAGB)[2] and one non-randomized study was limited to malabsorptive Roux-en-Y gastric bypass (RYGB).[8] The post-surgical groups were then compared with either their own pre-surgical pregnancies[7,9,11,12] or with other women who were pregnant but had not undergone bariatric surgery.[2,3,8,10,13-15]

Clinical Characteristics and Outcomes

Maternal characteristics and outcomes studied included: pre-pregnancy body mass index (BMI),[2,3,7-9,11-13] gestational weight gain,[2,11,12] pregnancy-induced hypertension,[3,7,8,13] pre-eclampsia,[2,3,8,11,12,14] gestational diabetes mellitus (GDM),[2,3,7,8,11-14] caesarean delivery rate,[2,3,14] emergency caesarean section,[8] induction of labour,[7,10,14] spontaneous abortion,[2] gastric band-related complications or adjustments,[2] maternal anemia,[7,10] post-partum hemorrhage,[10,14] acute abdominal pain,[8] maternal hospitalization time,[14] and adverse events and complications.[9,10,14]

Neonatal and child characteristics and outcomes studied included: birth weight,[2,3,7-11,14] small for gestational age,[2,3,7,15] large for gestational age/macrosomia,[2,3,10,15] gestational age,[3,7,9,14] frequency of pre-term birth,[2,3,15] congenital abnormality,[2,3,13] Apgar score,[7,10,14] admission to the neonatal intensive care unit (NICU),[2,8,14] perinatal mortality,[7,8,14,15] adverse events,[9,14] and BMI at 4 years,[11,12] 6 years,[11,12] and 10 years of age.[12]

Summary of Critical Appraisal

Both of the included systematic reviews used comprehensive literature search criteria and clearly presented the characteristics of the included studies;[2,3] however, the date limits for the literature search in the Vrebosch review were not provided.[2] It was unclear whether study selection or data extraction were done in duplicate.[2,3] Due to the heterogeneity of the studies included in the reviews, the results of the included studies were not combined statistically and were narratively summarized.[2,3] It was unclear whether study quality was assessed by Kjaer et al.[3] and, in the review by Vrebosch, et al.,[2] it was determined that the included studies were of low methodological quality due to their retrospective study design, limited sample sizes, and heterogeneous study populations. The Vrebosch review[2] included only studies that examined outcomes of women who had undergone restrictive bariatric procedures.

The authors of the nine non-randomized studies identified their study subjects from population-based[8,9,11-15] and hospital[7,10] databases. The data had been collected prospectively as part of routine hospital and population registry record keeping. Healthcare professionals caring for the women who were a part of these studies were not blinded to their surgical status. Therefore, it is possible that knowledge of previous bariatric surgery could have influenced some outcomes such as the mode of delivery. Other outcomes, such as birth weight are objective measures and are less likely to be compromised, but could also be influenced if patients who underwent bariatric surgery received different pre- or post-natal care.

In general, the study populations appeared to be representative of the populations of interest. By choosing subjects from population databases that included nearly the entire population, there was a low probability of missing potential subjects of interest to the authors. International Classification of Disease (ICD) codes were used to identified women who had undergone bariatric surgery and those who had been pregnant.[8,10-14] However, given that each study's population was focused in a single country, the results of the individual studies may have limited generalizability to populations in other geographic areas. Amsalem et al.[7] studied only women who had undergone restrictive bariatric procedures and Berlac et al.[8] studied only women who had undergone malabsorptive procedures. The results from these two studies may not be generalizable to those patients who have undergone other types of bariatric procedures.

In four of the non-randomized studies, [7,9,11,12] the impact of confounding factors on the study results was minimized by comparing obstetric and neonatal outcomes of the same women's pregnancies before and after they had undergone bariatric surgery. In the remaining non-randomized studies, confounding was minimized by matching pregnant women who had undergone bariatric surgery (cases) with pregnant women who had not undergone bariatric surgery (controls) based on a number of factors such as age, body mass index (BMI), and other pre-existing co-morbidities.[8,10,13-15] Multivariate logistic regression models were also used to adjust for confounding factors in the statistical analyses.[7,10,13] The authors of two studies indicated that the large sample sizes of their studies contributed to their good statistical power[8,13] while the small sample sizes of four studies may have reduced their statistical power and reliability of their results.[9,11,12,15]

Summary of Findings

Total gestational weight gain and maternal BMI were significantly greater in pregnancies before bariatric surgery.[11] The review by Vrebosch[2] concluded that gestational weight gain was lower in pregnancies following LAGB than for obese or normal weight women who became pregnant without surgery.

The conclusions of the systematic reviews[2,3] suggested that the risk of developing GDM was reduced following bariatric surgery. The Vrebosch review[2] concluded that the incidence of hypertension, pre-eclampsia, and caesarean section were lower following restrictive bariatric surgery when compared with obese controls but were higher than in normal weight controls. Hypertensive disorders were experienced significantly more often by women during pregnancies before restrictive bariatric surgery than during their first or second post-surgical pregnancy.[7] Hypertension rates were significantly greater in women who had undergone RYGB, as compared to pregnant women with a normal BMI but were similar to those reported in the adipose control group.[8] Berlac at al.[8] found that women who had undergone RYGB did not have a significantly different risk of pre-eclampsia as compared to normal weight controls. There was no statistically significant difference in pre-eclampsia rates between groups in one study.[14]

Gestational diabetes was experienced significantly more often by women during pregnancies before bariatric surgery than during their first[7,11,15] or second[7] post-surgical pregnancy. There was an increased risk of GDM for women who had undergone RYGB as compared to pregnant women with a normal BMI.[8] The odds of developing GDM were significantly greater for obese women than for those who had undergone bariatric surgery.[10] There was no statistically significant difference in GDM rates between groups in one study.[14]

One study found that labour was induced significantly more often in women who had had surgery as compared to obese controls.[10] Two studies found no significant difference in labour induction or caesarean section rates between groups.[7,14] The rate of spontaneous abortion was reported to be higher for the LAGB group than for either non-surgical control group in one study included in the Vrebosch review.[2] The difference between groups was not found to be statistically significant.

Post-delivery hemoglobin levels were significantly lower following women's second post-surgical pregnancy as compared to their pre-surgical pregnancy.[7] There was no significant difference observed when comparing the pre-surgical pregnancies with the first post-surgical pregnancy. Shai et al.[10] found the odds of post-partum anemia to be significantly higher for women following bariatric surgery as compared to obese controls. There was no statistically significant difference in post-partum hemorrhage rates between groups in one study.[14] An increased risk of acute abdominal pain was observed in women who had undergone RYGB as compared to pregnant women with a normal BMI.[8]

There was no significant difference in gestational age found between groups in one study.[9] Berlac et al.[8] found children born to mothers who had undergone RYGB had a lower birth weight than those born to normal weight mothers. Shai et al.[10] found the birth weight of newborns born after surgery was significantly less than those whose mothers were obese. The Kjaer study[14] found the mean birth weight of babies born after bariatric surgery was significantly less than those whose mothers had not had surgery. Three studies[7,11,15] found that birth weight was significantly greater for offspring born from pregnancies before bariatric surgery than those born to the same mothers after surgery while Dell'Angnolo et al.[9] found no significant differences in the birth weight of newborns born to the same woman before and after bariatric surgery. No significant differences were found in birth weight between groups in one study.[8]

In the review by Kjaer,[3] birth weight and macrosomia were not different between surgical and non-surgical groups in six of eight studies and in the Vrebosch review,[2] the incidence of macrosomia and low birth weight were lower in the LAGB group than in obese women. The Kjaer review[3] found the risk of small-for-gestational age infants was significantly higher only when compared with non-obese or severely obese controls. The Kjaer[14] and Roos[15] studies found the odds were significantly greater for infants born to mothers who had undergone surgery to be small-for-gestational age.

In one review,[2] the rate of pre-term deliveries was reported to be higher in the LAGB group than in the normal weight control group. The same results were found by Roos et al.[15] when comparing women after any bariatric surgery with those who had not had surgery. No significant differences were found between groups in two studies.[7,14]

The Kjaer review[3] identified one study that suggested there was a higher risk of birth defects following bariatric surgery and six studies that identified no additional risk. The study by Josefsson[13] found that an increased risk of congenital malformation was not associated with pregnancies following bariatric surgery but the risk did increase significantly as the mothers' BMI increased. Berlac et al.[8] found no statistically significant difference in congenital malformations between groups.

There was no significant difference in NICU admission rates between groups in the review by Vrebosch[2] or in the study by Kjaer.[14] Berlac et al.[8] found that babies born to mothers in the surgical group had a significantly lower risk of being admitted to the NICU and of illness in the neonatal period when compared to babies born to mothers of normal weight. Asphyxia of the newborn was significantly more common in the obese control group as compared to mothers who had undergone surgery.[8] There were no significant differences identified between groups in terms of still birth,[15] or neonatal or perinatal death.[14,15]

The BMI of offspring born to the same mothers before and after bariatric surgery were not significantly different at 4 years[11,12] and 6 years[11,12] of age. At 10 years of age, the BMI of children born after bariatric surgery, particularly girls, was significantly greater than the BMI of those who were born before surgery.[12]

Limitations

It should be noted that the included studies undertaken in the same countries may represent some duplication of results. The two studies conducted in Israel[7,10] both included bariatric and obstetric patients from the same hospital. The Danish studies[8,14] both relied on the Danish National Patient Register and the Danish Medical Birth Registry to identify their subjects and obtain their data for analysis. The four studies conducted in Sweden[11-13,15] all drew information from the Swedish Medical Birth Register. The non-randomized study that was conducted in Brazil[9] is the only one without duplication. Additionally, none of the identified studies included a North American population. This may limit the generalizability of the studies' conclusions to a Canadian population. Studies that did not separate the results of restrictive and malabsorptive surgical procedures[3,7,9-15] do not allow us to determine the outcomes related specifically to either type of procedure. The clinical significance of some findings, such as variations in birth weight remain unclear.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

The results of the studies included in this review generally suggested that pregnancy after bariatric surgery, both restrictive and malabsorptive, was safe for mother and child. There were some positive effects observed on potential maternal and neonatal outcomes that could be impacted by BMI.[2] In before and after studies, there was a significant decrease in pregnancy complications,[7] pregnancy was determined to be safe, and newborn birth weight was not compromised.[9] Generally, there was no effect observed of bariatric surgery on childhood weight of offpring.[11,12] When compared with obese controls, pre-eclampsia was improved following surgery.[8] Hypertension, GDM, and acute abdominal pain remained more common following surgery when compared to normal weight controls.[8] When compared to BMI-matched controls, women who had undergone surgery were at increased risk for preterm or small babies.[14,15] There was no evidence to indicate that there was an increased risk of congenital malformation for children born following bariatric surgery.[3,8,13] The authors generally concluded that additional larger studies may be required before a definitive conclusion regarding safety can be made.

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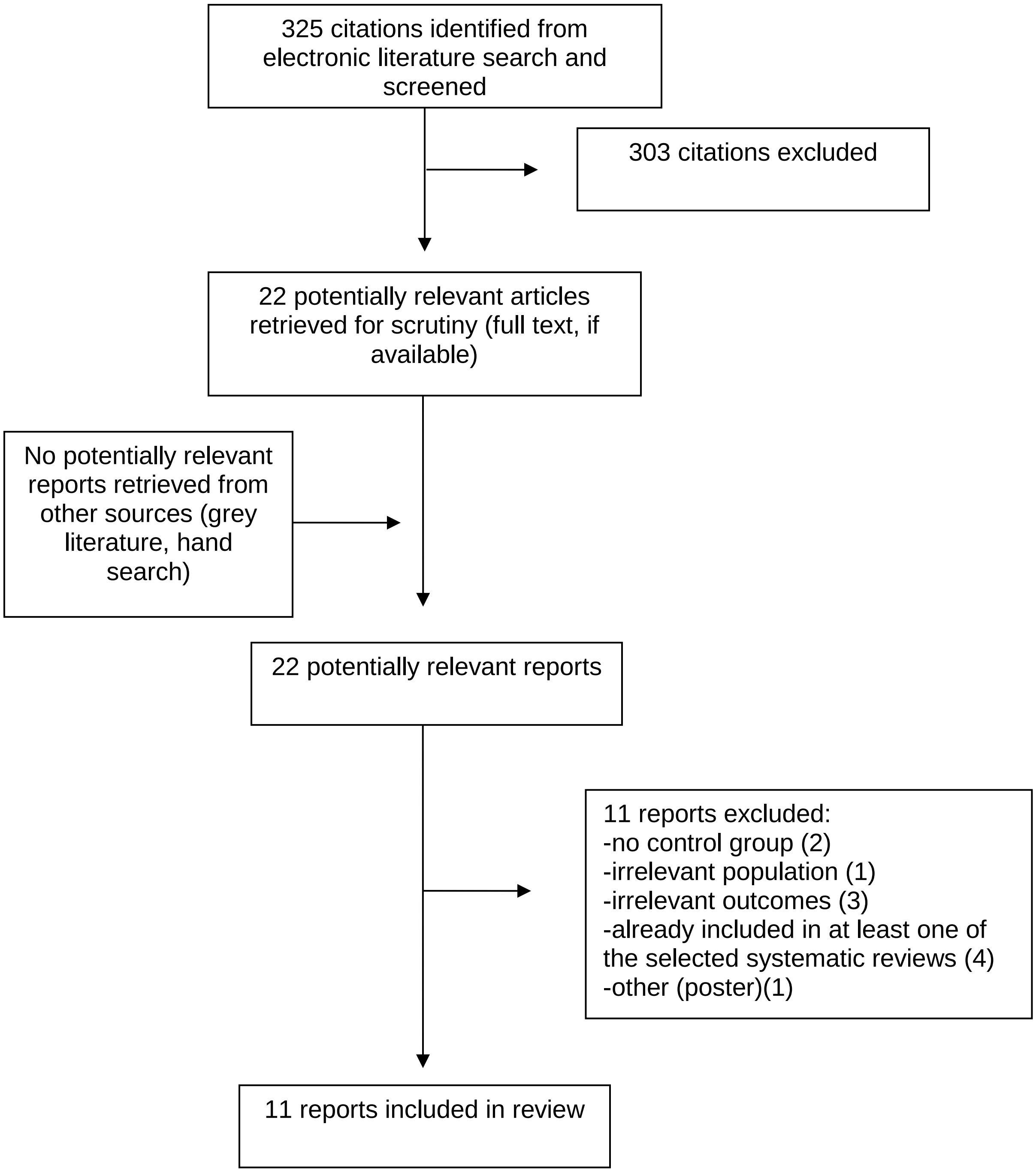
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Characteristics of Included Publications

Table A1: Characteristics of Included Systematic Reviews and Meta-Analyses					
Objectives, Scope	**Types of primary studies included**	**Population Characteristics**	**Intervention**	**Comparator(s)**	**Clinical Outcomes, Length of Follow-Up**
Kjaer, 2012[3]					
A review of benefits and risks associated with pregnancy after bariatric surgery	17 studies included, study types not specified	Combined population characteristics not provided	Pregnancy following bariatric surgery (malabsorptive and restrictive)	Pregnancy without bariatric surgery	<u>maternal</u> PIH, pre-eclampsia, eclampsia, GDM, and mode of delivery <u>neonatal</u> birth weight, SGA, LGA/macrosomia, gestational age, preterm birth, and birth defects
Vrebosch, 2012[2]					
To identify maternal and neonatal outcomes in pregnancy following LAGB	four observational studies with control group, seven observational studies without control group case reports excluded	728 LAGB pregnancies in 638 women	Pregnancy following LAGB	Pregnancy without bariatric surgery	<u>maternal</u> band-related complications or adjustments, mean GWG, GDM, PIH, pre-eclampsia, caesarean delivery rate <u>neonatal</u> preterm delivery, low birth weight, high birth weight, LGA, SGA, spontaneous abortion, congenital abnormalities, admission to NICU

GDM = gestational diabetes mellitus; GWG = gestational weight gain; LAGB = laparoscopic adjustable gastric banding; LGA = large for gestational age; NICU = neonatal intensive care unit; PIH = pregnancy-induced hypertension; SGA = small for gestational age

Table A2: Characteristics of Included Clinical Studies					
First Author, Publication Year, Country	**Study Design**	**Patient Characteristics**	**Intervention(s)**	**Comparator(s)**	**Clinical Characteristics and Outcomes**
Amsalem, 2014[7] Israel	Retrospective population-based cohort study comparing pregnancy outcomes of women before and after bariatric surgery Soroka University medical Center	109 women who had conceived before and at least twice after bariatric surgery between 2006 and 2012 327 paired pregnancies (109 before surgery, 218 following surgery)	Pregnancy following restrictive bariatric surgery	Pregnancy prior to bariatric surgery	<u>Maternal</u> age, gravidity, parity, BMI before pregnancy, BMI before delivery, BMI before bariatric procedure, smoking status, type of bariatric surgery, hypertensive disorders, pregestational diabetes, gestational diabetes, infections during pregnancy, labor induction, maternal anemia <u>Newborn</u> gestational age, intrauterine growth restriction, gender, birth weight, Apgar score, perinatal mortality
Berlac, 2014[8] Denmark	Retrospective population-based cohort study comparing pregnancy outcomes of women following bariatric surgery with normal weight and overweight controls	415 singleton deliveries underwent RYGB surgery between 1996 and 2011 were matched to 829 normal weight and 826 adipose controls who had not had bariatric surgery (1	Pregnancy following RYGB surgery	Pregnancy without bariatric surgery (normal weight or overweight)	<u>Maternal</u> BMI, hypertension in pregnancy, gestational diabetes mellitus, acute abdominal pain, pre-eclampsia, emergency caesarean section

Table A2: Characteristics of Included Clinical Studies					
First Author, Publication Year, Country	**Study Design**	**Patient Characteristics**	**Intervention(s)**	**Comparator(s)**	**Clinical Characteristics and Outcomes**
	Danish National Patient Register and the Danish Medical Birth Registry	intervention to 4 controls)			Newborn asphyxia, birth weight, admissions to NICU
Dell'Angnolo, 2014[9] Brazil	Retrospective cohort study comparing maternal and newborn outcomes before and after maternal bariatric surgery	32 women who had undergone bariatric surgery between 1999 and 2008 and became pregnant following surgery. 11 women had one or more children prior to bariatric surgery.	Pregnancy following bariatric surgery	Pregnancy prior to bariatric surgery	Maternal Pre-pregnancy BMI, adverse events Newborn Birth weight, gestational age, adverse events
Shai, 2014[10] Israel	Retrospective database study to evaluate pregnancy outcome and rates of anemia in women following bariatric surgery in comparison with obese pregnant women Soroka University medical Center between 1988 and 2010	326 women who had undergone bariatric surgery and delivered before and after surgery between 1988 and 2010 at a single centre. 1612 obese women without bariatric surgery who had at least two deliveries during the same time period	Pregnancy following bariatric surgery	Pregnancy in obese women without bariatric surgery	Maternal pregnancy and labor complications (induction of labor, dystocia, anemia, postpartum hemorrhage, and wound infection) Perinatal birth weight, macrosomia (≥4 kg), low Apgar scores (<7) at 1 and 5 minutes
Berglind, 2013[11] Sweden	Retrospective database study comparing BMI of offspring born to	124 women who had undergone bariatric surgery between 1980 and 2006 and had	Pregnancy following bariatric surgery	Pregnancy prior to bariatric surgery	Maternal BMI during pregnancies, BMI at time of bariatric

Table A2: Characteristics of Included Clinical Studies					
First Author, Publication Year, Country	**Study Design**	**Patient Characteristics**	**Intervention(s)**	**Comparator(s)**	**Clinical Characteristics and Outcomes**
	mothers before and after maternal bariatric surgery Swedish Medical Birth Register	given birth before and after surgery. 39 sibling pairs with complete information			surgery, post-surgical BMI, GWG, mean rate of gain in gestational weight per week, gestational diabetes, pre-eclampsia, breastfeeding, smoking status Children Birth weight and length, BMI at 4 and 6 years
Willmer, 2013[12] Sweden	Retrospective database study comparing BMI of offspring born to mothers before and after maternal bariatric surgery Swedish Medical Birth Register	223 women with at least one child each who had undergone bariatric surgery between 1980 and 2008. 71 families (child-woman-child triads) with complete information	Pregnancy following bariatric surgery	Pregnancy prior to bariatric surgery	Maternal BMI during pregnancies, BMI at time of bariatric surgery, post-surgical BMI, GWG, mean rate of gain in gestational weight per week, gestational diabetes, pre-eclampsia, breastfeeding, smoking status Children BMI at 4 years of age predicted using statistical regression

Table A2: Characteristics of Included Clinical Studies					
First Author, Publication Year, Country	**Study Design**	**Patient Characteristics**	**Intervention(s)**	**Comparator(s)**	**Clinical Characteristics and Outcomes**
Josefsson, 2013[13] Sweden	Retrospective study of prospectively collected, population-based register Swedish Medical Birth Register	All firstborn children born before 2010 to women born between 1973 to 1983 were studied to determine if they had a congenital abnormality and a mother who had undergone bariatric surgery before pregnancy (n = 318) No surgery (n = 244,294)	Pregnancy following bariatric surgery	Pregnancy without bariatric surgery	<u>Maternal</u> marital or cohabitation status, smoking, BMI, diabetes, and hypertension during pregnancy <u>Newborns</u> Congenital malformations
Kjaer, 2013[14] Denmark	Retrospective register-based matched cohort study Aim – describe the risk of adverse maternal and neonatal outcome following bariatric surgery Danish National Patient Register and the Danish Medical Birth Registry	339 women with singleton delivery following bariatric surgery between 2004 and 2010 were matched to 1277 women with singleton delivery who had not had bariatric surgery (1 intervention to 4 controls)	Pregnancy following bariatric surgery	Pregnancy without bariatric surgery	<u>Maternal</u> Gestational diabetes mellitus, pre-eclampsia, labor induction, caesarean section, post-partum hemorrhage, maternal hospitalization time, complications <u>Neonatal</u> Gestational age, birth weight, Apgar score, admission to NICU, perinatal death, complications
Roos, 2013[15] Sweden	Population-based matched cohort study to compare perinatal	Births to a mother with a history of bariatric surgery (n = 2511)	Pregnancy following bariatric surgery	Pregnancy without bariatric surgery	Pre-term birth, small for gestational age, large for gestational

Table A2: Characteristics of Included Clinical Studies					
First Author, Publication Year, Country	**Study Design**	**Patient Characteristics**	**Intervention(s)**	**Comparator(s)**	**Clinical Characteristics and Outcomes**
	outcomes in births of women with versus without a history of bariatric surgery Swedish Medical Birth Register	between 1992 and 2009 were matched with up to 5 controls (n = 12,379) based on maternal age, early pregnancy BMI, early pregnancy smoking status, educational level, and year of delivery Secondary control cohorts included women eligible for bariatric surgery (BMI ≥35 or ≥40) and were matched on the same factors except for BMI			age, still birth, (≥28 weeks) and neonatal death (0 to 27 days)

BMI = body mass index; GWG = gestational weight gain; kg = kilogram; NICU = neonatal intensive care unit; RYGB = Roux-en-Y gastric bypass

APPENDIX 3: Critical Appraisal of Included Publications

Table A3: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[5]

Strengths	Limitations
Kjaer, 2012[3]	
• Comprehensive literature search undertaken • Characteristics of included studies clearly presented • No conflicts of interest were declared	• Unclear whether study selection and data extraction were done in duplicate • Quality of included studies was not assessed • There was heterogeneity in design, type of surgery, number of cases and control groups • Results of the various studies were not combined and were presented only narratively
Vrebosch, 2012[2]	
• Comprehensive literature search undertaken • Characteristics of included studies clearly presented • Conflict of interest statement provided	• Date limits of literature search not provided • Unclear whether study selection and data extraction were done in duplicate • Included studies indicated to be of low methodological quality • Results of the various studies were not combined and were presented only narratively

Table A4: Strengths and Limitations of Non-Randomized Studies using Downs and Black[6]

Strengths	Limitations
Amsalem, 2014[7]	
• Objective clearly stated • population well described and determined not to be significantly different from previous populations of women with only one post-bariatric pregnancy • confounding factors minimized by selecting paired deliveries from the same woman • Serves as their own control • Multivariate models used to adjust for confounding factors • study population chosen from a single hospital that serves the majority of the obstetric population in the area • data was gathered prospectively; minimizes recall bias	• retrospective population-based cohort • Results may not be generalizable to women who have undergone malabsorptive bariatric procedures • population chosen from a limited geographical area; may reduce the generalizability of the findings to other populations
Berlac, 2014[8]	
• inclusion of all Danish women undergoing bypass who became pregnant in the time period (based on medical charting codes) • near complete follow up by retrieving data from the birth register • large number of exposed and unexposed controls • data was gathered prospectively; minimizes recall bias	• retrospective population-based cohort • RYGB results may not be generalizable to restrictive procedures • Did not adjust for confounders through regression analysis, only through matching of cases and controls • validity of diagnoses of some obstetrical complications not 100% and may under estimate risk differences

Table A4: Strengths and Limitations of Non-Randomized Studies using Downs and Black[6]	
Strengths	**Limitations**
	• Did not include information regarding smoking status • population chosen from a limited geographical area; may reduce the generalizability of the findings to other populations
Dell'Angnolo, 2014[9]	
• Some data taken from existing, prospectively completed medical records • Examine the same women before and after bariatric intervention; served as their own controls • statistical analyses used to assess association were well described	• retrospective study design • some data collected through interviews; may introduce recall bias • small sample size may limit generalizability and statistical power • population chosen from a limited geographical area; may reduce the generalizability of the findings to other populations
Shai, 2014[10]	
• compared the same women before and after bariatric surgery, as well as with controls with the same number of pregnancies • women identified by medical chart coding; reduces selection bias • multivariate logistic regression used to control for confounders	• retrospective study design • did not distinguish between different types of bariatric procedures • population chosen from a limited geographical area; may reduce the generalizability of the findings to other populations
Berglind, 2013[11]	
• adjusted for confounding in terms of social and lifestyle factors of mothers by comparing the same women before and after bariatric procedures • women identified by medical chart coding from a national database; may reduce selection bias	• Large drop-out due to incomplete information • Small sample size reduced statistical power • Low statistical power may have impacted results • Reliance on national register may have resulted in non-differential misclassification • Study population was chosen from a limited geographical area; may reduce the generalizability of the findings to other populations
Josefsson, 2013[13]	
• Subjects chosen from comprehensive national registry using ICD codes to determine inclusion • statistical methods used were well described • large sample size provided good statistical power • statistical analysis was adjusted for confounders	• determined outcome before determining cause • some maternal height and weight data missing from the registry and measurements were not standardized • population chosen from a limited geographical area; may reduce the generalizability of the findings to other populations
Kjaer, 2013[14]	
• Controls were matched to subjects based on BMI, maternal age, parity, and date of delivery but otherwise chosen randomly from the sample population • Subjects chosen from comprehensive national registry using ICD codes to determine inclusion •	• population chosen from a limited geographical area; may reduce the generalizability of the findings to other populations

Table A4: Strengths and Limitations of Non-Randomized Studies using Downs and Black[6]	
Strengths	**Limitations**
Roos, 2013[15]	
• representative of the population of interest (included 95% of the population in Sweden) • outcomes data recorded prospectively which minimizes recall bias	• lack of information regarding women's pre-surgery weight and weight loss between surgery and pregnancy • database used only captures 84% of bariatric procedures in Sweden – possibly exposure misclassification • population chosen from a limited geographical area; may reduce the generalizability of the findings to other populations • the small number of mortality events in the large sample size resulted in low statistical power for that outcome
Willmer, 2013[12]	
• adjusted for confounding in terms of social and lifestyle factors of mothers by comparing the same women before and after bariatric procedures • women identified by medical chart coding from a national database; may reduce selection bias • children's outcomes were retrieved from medical charts	• Large drop-out due to incomplete information • Small sample size reduced statistical power • Low statistical power may have impacted results • Reliance on national register may have resulted in non-differential misclassification • Study population was chosen from a limited geographical area; may reduce the generalizability of the findings to other populations

ICD = International Classification of Diseases; RYGB = Roux-en-Y gastric bypass

APPENDIX 4: Main Study Findings and Conclusions

Table A5: Summary of Findings of Included Studies	
Main Study Findings	**Conclusions**
Kjaer, 2012[3]	
• Birthweight and risk of macrosomia were not different between groups following bariatric surgery in six of eight studies • Higher risk of small-for-gestational age infants was reported in five studies, but the risk was only significant when compared with non-obese women or severely obese controls • No differences were reported in gestational length • One study indicates a higher risk of birth defects following bariatric surgery and six studies reported no difference in risk • The risk of developing pre-eclampsia or gestational diabetes mellitus was reduced following bariatric surgery	• The results suggest pregnancy following bariatric surgery is safe • Additional studies matching cases and controls on the basis of BMI may be required
Vrebosch, 2012[2]	
• Gestational weight gain was lower in pregnancies after LAGB than in obese or normal weight women who became pregnant without surgery • The incidence of gestational diabetes was reported to be lower in pregnancies following LAGB than in pregnancies of obese women without surgery • Incidence of gestational hypertension, pre-eclampsia, and caesarean section were lower following surgery when compared to pregnancies of obese women but higher than in normal weight women who had not had surgery • The rate of pre-term deliveries was reported to be higher in the LAGB group than in those women who were of normal weight without surgery • Incidence of macrosomia or low birth weight was lower in the LAGB group than in obese women without surgery • The rate of spontaneous abortion was higher in the LAGB group than in either non-surgical group • There was no significant difference in NICU admission rate between groups.	• Pregnancy following LAGB appears to be safe and have a positive effect on potential maternal and neonatal outcomes that could be impacted by BMI • Additional larger studies may be required before a definitive conclusion can be made.
Amsalem, 2014[7]	
<u>Hypertensive disorders</u> Before surgery = 21.0% First delivery after surgery = 7.4% Second delivery after surgery = 4.7% • before vs first (*P* <0.01)	• There were no significant differences reported in clinical characteristics between pregnancies before and after bariatric surgery in terms of intrauterine growth, polyhydraminos, oligohydraminos, induction of labour, or

Table A5: Summary of Findings of Included Studies	
Main Study Findings	**Conclusions**
• before vs second (P <0.01) • first vs second (P = 0.687) Gestational diabetes mellitus Before surgery = 19.0% First delivery after surgery = 5.6% Second delivery after surgery = 6.6% • before vs first (P <0.01) • before vs second (P <0.05) • first vs second (P = 0.999) Augmentation of labour Before surgery = 28.8% First delivery after surgery = 18.8% Second delivery after surgery = 15.4% • before vs first (P = 0.099) • before vs second (P <0.05) • first vs second (P = 0.690) Post-delivery hemoglobin (mean ± SD) Before surgery = 10.7 ± 1.3 First delivery after surgery = 10.4 ± 1,5 Second delivery after surgery = 10.3 ± 1.4 • before vs first (P = 0.166) • before vs second (P <0.05) • first vs second (P = 0.506) Birth weight (kg ± SD in g) Before surgery = 3.3 ± 642 First delivery after surgery = 3.1 ± 666 Second delivery after surgery = 3.1 ± 441 • before vs first (P <0.05) • before vs second (P <0.05) • first vs second (P = 0.905) Macrosomia Before surgery = 11.1% First delivery after surgery = 7.1% Second delivery after surgery = 1.1% • before vs first (P = 0.581) • before vs second (P <0.05) • first vs second (P = 0.219)	malpresentation. • There were no significant differences reported in clinical characteristics of deliveries before and after bariatric surgery in terms of pre-term delivery, caesarean section, or Apgar score less than 7 at one or five minutes. • improvement in pregnancy complications (hypertensive disorders and gestational diabetes mellitus) were maintained following the second post-surgical pregnancy • “a significant decrease in pregnancy complications, such as hypertensive disorders and GDM, is achieved after bariatric surgery.”p. 449
Berlac, 2014[8]	
Hypertension in pregnancy (%) Bariatric = 19 (4.6) Obese = 52 (6.3) Normal = 15 (1.8) • bariatric vs normal P <0.01 Gestational diabetes mellitus (%)	• “we found a significantly increased risk of hypertension in pregnancy, gestational diabetes and acute abdominal pain among women who had undergone an RYGB procedure as compared with women with a normal BMI.” p. 450 • “children born to women after RYGB surgery

Table A5: Summary of Findings of Included Studies	
Main Study Findings	**Conclusions**
Bariatric = 38 (9.2) [RR 6.9; 95% CI, 3.5 to 13.5] Obese = 67 (8.1) Normal = 11 (1.3) • bariatric vs normal *P* <0.001 <u>Birth weight difference vs reference (g)</u> Bariatric = –212 Obese = 107 • bariatric vs normal *P* <0.001 • obese vs bariatric *P* <0.001 <u>Admittance to NICU (%)</u> Bariatric = 83 (20.1) [RR 1.5; 95% CI, 1.1 to 2.0] Obese = 136 (16.6) Normal = 112 (13.5) • bariatric vs normal *P* <0.01 <u>Illness in neonatal period (%)</u> Bariatric = 137 (33.1) [RR 1.3, 95% CI 1.0 to 1.6] Obese = 274 (33.2) Normal = 217 (26.2) • bariatric vs normal *P* <0.05 <u>Asphyxia in newborn (%)</u> Bariatric = 10 (2.4) Obese = 48 (5.8) Normal = 33 (4.0) • obese vs bariatric *P* <0.01	had a lower birth weight than the normal weight control group and a significantly decreased risk of being admitted to neonatal intensive care unit, when compared with babies born to normal weight mothers." p.451 • The bariatric group did not have a significantly higher incidence of pre-eclampsia when compared with the normal weight controls • No statistically significant differences were observed between groups in regards to gestational age, birth weight, Apgar score at 5 minutes, or congenital malformations.
Dell'Angnolo, 2014[9]	

N = 32
 	
<u>Time to pregnancy following bariatric surgery (%)</u>
>2 years = 19 (59.38)
1 to 2 years = 11 (34.38)
Within 1 year = 2 (6.25)
 	
• No statistical association between:
  o birth weight and maternal BMI (Chi-square, *P* = 0.21; Fisher's, *P* = 0.23)
  o birth weight and time between surgery and pregnancy (Chi-square, *P* = 0.08; Fisher's, *P* = 0.11)
  o gestational age and low birth weight (Chi-square, *P* = 0.29; Fisher's, *P* = 0.28)
• no statistically significant difference in birth weight of newborns of women who had children before or after bariatric procedure (Chi-square, *P* = 0.5286; Fisher's, *P* = 0.4239)
	• "main conclusion was that there was no difference in newborn outcomes when comparing pregnancies before and after the performance of bariatric surgery." p.701

Shai, 2014[10]	

Table A5: Summary of Findings of Included Studies	
Main Study Findings	**Conclusions**
Gestational diabetes mellitus (%) Bariatric = 33 (10.1) Obese = 237 (14.7) OR 0.6; 95% CI, 0.44 to 0.9; *P* = 0.029 • other obstetric risk factors of pregnancies with previous bariatric surgery and with obesity (previous caesarean section, chronic hypertension, mild or severe pre-eclampsia, and fertility treatment) were not significantly different between groups. Induction of labour (%) Bariatric = 116 (35.6) Obese = 458 (28.4) OR 1.3; 95% CI, 1.08 to 1.7; *P* = 0.010 Birth weight (mean ± SD) Bariatric = 3206 ± 495 g Obese = 3454 ± 539 g *P* <0.001 Post-partum anemia (Hb < 10 g/dL) (%) Bariatric = 157 (48.2) Obese = 609 (37.8) OR 1.5; 95% CI, 1.2 to 1.9; *P* = <0.001 Macrosomia (birth weight <4 kg) (%) Bariatric = 323 (4.4) Obese = 1363 (13.4) OR 0.3; 95% CI, 0.17 to 0.61; *P* = <0.001 • other pregnancy and labor characteristics in pregnancies with bariatric surgery and with obesity (dystocia at 1st or 2nd stage, post-partum hemorrhage, blood transfusion, wound infection, and Apgar score <7)	• "…previous bariatric surgery is an independent protective." p.277 • following bariatric surgery, mothers were less likely to give birth to large newborns than obese women who had not had bariatric surgery
Berglind, 2013[11]	
• Birth weight was significantly different between offspring born before and after bariatric surgery Birth weight(SD) 3.7 kg (0.7) vs 3.5 kg (0.6) (*P* = 0.002) • Gestational diabetes occurred in 2.4% of pregnancies before bariatric surgery and none after surgery (*P* <0.001) • Offspring BMI at 4 and 6 years were not significantly different between the before and after groups (*P* = 0.060 and *P* = 0.23)	• There were positive, but not statistically significant, associations detected between gestational weight gain and mean growth rate during each trimester on child's birth weight • Total GWG and second semester weight gain were positively associated with birth weight • No associations were found with BMI in pre-school age

Table A5: Summary of Findings of Included Studies	
Main Study Findings	**Conclusions**
• Total GWG and maternal BMI were significantly different before and after bariatric surgery GWG (SD) 11.3 kg (7.2) vs 8.3 (6.4) (*P* <0.001) Maternal BMI at birth (SD) 40.7 (4.5) vs 34.2 (6.3) (*P* <0.001)	
Josefsson, 2013[13]	
Congenital malformation (%) Bariatric = 13 (4.1); 95% CI, 2.2 to 6.0 No surgery = 8282 (3.4%); 95% CI, 3.3 to 3.5 Adjusted odds ratios for congenital malformation Bariatric surgery before pregnancy = 1.09 (95% CI, 0.63 to 1.91, *P* = 0.747) Maternal BMI between 25 and 29 kg/m^3 = 1.09 (95% CI, 1.03 to 1.15, *P* = 0.003) Maternal BMI between 30 and 34 kg/m^3 = 1.14 (95% CI, 1.05 to 1.24, *P* = 0.002) Maternal BMI ≥35 kg/m^3 = 1.30 (95% CI, 1.16 to 1.45, *P* <0.001)	• bariatric surgery did not have any effect on the odds ratio for having congenital malformation but a high to very high BMI does appear to increase the risk • authors suggest pregnant women with bariatric surgery should be treated as a group at risk
Kjaer, 2013[14]	
Exposed n = 339 Unexposed n = 1277 Surgical procedure (%) RYGB = 286 (83.4) Gastric banding = 57 (16.6) Median time from surgery to birth = 629 days (range = 93 to 3452 days) • Exposed and unexposed significantly different only in terms of current smoking status (21.2% vs 14.6%, *P* <0.01) Mean gestational age Exposed = 274 days Unexposed = 278 days *P* <0.001 • Frequency of preterm birth (<37 weeks) and birth after 42 weeks were not significantly different between groups Mean birth weight Exposed = 3312 g (± 594) Unexposed = 3585 g (± 649) *P* <0.001 SGA (-2SD) Exposed = 7.1% (24)	• Higher risk of SGA for infants born after bariatric surgery after adjusting for confounding factors

Table A5: Summary of Findings of Included Studies	
Main Study Findings	**Conclusions**
Unexposed = 2.9% (37) (OR = 2.29; 95% CI 1.33 to 3.96; *P* <0.01) <u>LGA (+2SD)</u> Exposed = 2.4% (8) Unexposed = 7.3% (93) (OR = 0.31; 95% CI 0.15 to 0.65; *P* <0.01) • There were no statistically significant differences between groups in the frequency of maternal and neonatal complications (GDM, pre-eclampsia, labour induction, caesarean section, postpartum hemmorhage, 5 minute Apgar score <7, NICU admission, or perinatal death)	
Roos, 2013[15]	
<u>Preterm births (%)</u> Bariatric = 243 (9.7) No surgery = 750 (6.1) OR 1.7; 95% CI 1.4 to 2.0, *P* <0.001 <u>Spontaneous preterm birth (%)</u> Bariatric = 130 (5.2) No surgery = 441 (3.6) OR 1.5; 95% CI 1.2 to 1.9, *P* <0.001 <u>Medically indicated preterm birth (%)</u> Bariatric = 113 (4.5) No surgery = 309 (2.5) OR 1.8; 95% CI 1.4 to 2.3, *P* <0.001 <u>Small for gestational age birth (%)</u> Bariatric = 131 (5.2) No surgery = 369 (3.0) OR 2.0; 95% CI 1.5 to 2.5, *P* <0.001 <u>Large for gestational age birth (%)</u> Bariatric = 105 (4.2) No surgery = 895 (7.3) OR 0.6, 95% CI 0.4 to 0.7, *P* <0.001 • no significant differences between groups in terms of still birth or neonatal death.	• Body mass appeared to be an effect modifier (*P* = 0.01) • Previous history of bariatric surgery increased the odds preterm birth and small for gestational age and decreased the odds of large for gestational age • these results remained the same when women with history of surgery were compared with those women eligible for surgery
Willmer, 2013[12]	
• Birth weight was significantly different between offspring born before and after bariatric surgery <u>Adjusted birth weight(SD)</u> 3.7 kg (0.7) vs 3.5 kg (0.6) (*P* = 0.002) • Gestational diabetes occurred in 2.4% of pregnancies before bariatric surgery and none	• There were positive, but not statistically significant, associations detected between gestational weight gain and mean growth rate during each trimester on child's birth weight • Total GWG and second semester weight gain were positively associated with birth weight • No associations were found with BMI in pre-

Table A5: Summary of Findings of Included Studies	
Main Study Findings	**Conclusions**
after surgery (P <0.001) • Adjusted offspring BMI at 4 and 6 years were not significantly different between the before and after groups (P = 0.117 and P = 0.072) but BMI was significantly greater in 10 year olds born after bariatric surgery (P = 0.038) • The prevalence of overweight children before and after surgery was not significantly different between groups at 4, 6 or 10 years of age. • When stratified by procedure type, there were no significant differences in the results	school age • The prevalence of obesity in 10 year olds (particularly girls) was significantly greater in children born to mothers following bariatric surgery.

BMI = body mass index; CI = confidence interval; dL = deciliter; g = grams; GDM = gestational diabetes mellitus; GWG = gestational weight gain; Hb = hemoglobin; kg = kilograms; LAGB = laparoscopic adjustable gastric banding; NICU = neonatal intensive care unit; OR = odds ratio; RR = relative risk; SD = standard deviation; SGA = small for gestational age