A Systematic Review of the effects of pre-pregnancy weight loss on perinatal outcomes among overweight and obese mothers

Abstract

Background: Obesity has become an increasing health problem in the US over the past several decades, and is associated with health problems in all populations. Studies investigating the effects of obesity on pregnancy have shown an increase in adverse perinatal outcomes.

Purpose: To review the literature on the effects of pre-pregnancy weight loss on perinatal outcomes among overweight and obese mothers.

Data sources: PubMed and ISI Web of Knowledge were searched for relevant articles from 4/10/2011 to 5/23/2011; previous reference lists were reviewed to find other relevant studies.

Data extraction: The review of the literature included 1021 abstracts and 55 full-text articles. Ten studies were included.

Study selection: Studies deemed to have "good" and "fair" internal validity were included in analysis.

Data synthesis: The evidence presents a mixed picture. Many studies were not significantly powered to produce statistically significant differences in outcomes. Although it does appear that pre-pregnancy weight loss may be associated with a decrease in preeclampsia and macrosomia, the effects on preterm birth, cesarean section, intrauterine growth restriction, low birth weight, and perinatal mortality are unclear. More high quality studies are needed to elucidate the effects of pre-pregnancy weight loss on these perinatal outcomes.

Conclusion: While it appears that pre-pregnancy weight loss may be associated with a decrease in preeclampsia and macrosomia, the evidence is ultimately insufficient to determine the effects of pre-pregnancy weight loss on other perinatal outcomes.

A Systematic Review of the effects of pre-pregnancy weight loss on perinatal outcomes among overweight and obese mothers

Overweight and obesity are increasing health problems in the US and around the world. Furthermore, numerous health and birth problems are known to be associated with overweight and obese status. This systematic review investigates the effects of pre-pregnancy weight loss on perinatal outcomes among overweight and obese mothers.

Introduction

Over the past few decades, the startling trend of increasing weight and adiposity amongst the American population has rapidly become an obesity epidemic. Obesity is a public health problem that has quickly become one of the most common afflictions in the world. According to data from the National Health and Nutrition Examination Study (NHANES) accumulated from 1971 to 2008, the prevalence of overweight and obese populations has steadily increased over the last 30 years, to the point that the age-adjusted prevalence of overweight and obesity among adults aged 20 or older was 68.0%.[1] The changes associated with an increasingly unhealthy diet and decreased activity levels are just a few of the factors that account for the steady rise in weight and adiposity amongst almost all demographic groups in the United States. Now, obesity can be considered a public health emergency in the United States, a problem that is steadily increasing in severity without any immediate solution.

The health implications of obesity are widely known and have been heavily studied. Obesity is known to be a risk factor for many chronic conditions including diabetes, hypertension, hypercholesterolemia, stroke, heart disease, certain cancers, and arthritis.[1] As the rates of obesity continue to increase year after year, the incidence of these chronic diseases are projected to increase as well. If obesity continues to increase at its current rates, it is expected that health care costs due to conditions arising from obesity could range from 860.7 to 956.9 billion US dollars by the year 2030. This would be roughly equivalent to 1 of every 6 dollars spent on health care.[2] With increases in chronic health problems as a

result of obesity as well as increases in health care costs stemming from obese and overweight individuals, the issue of obesity has become a public health emergency.

In the area of women's health, the obesity epidemic is even more alarming. 2008 NHANES data shows that while a larger proportion of men than women are likely to be overweight or obese (72.3% vs. 64.1%, respectively), as individuals, women were still more likely than men to be obese (35.5% vs. 32.2%).[1] An analysis of all accumulated NHANES data (beginning with NHANES I in 1971-1974) also shows that the annual increase in weight as determined by Body Mass Index (BMI) has been substantially greater for women compared to men. In fact, women have an annual increase in BMI of 0.911 percentage points as compared to men who have an annual increase in BMI of 0.653 percentage points.[2] The same analysis projects that by the year 2030, 87.2% of US women will be overweight or obese. In some subgroups, the rates of overweight and obesity are alarmingly high; for example, the prevalence of overweight and obesity amongst African American women is already 78%.[2] Taken togethere, these facts indicate that obesity rates are rising amongst women and that consequently, women are at a greater risk for chronic conditions as a result of being overweight or obese.

In taking a closer look at the obese populations in women, NHANES data found that 59.5% of women of childbearing age, ages 20-39, are overweight and obese.[1] While this age range does not represent all women who become pregnant in the United States, it does represent the majority. With a growing number of women of reproductive age becoming obese and overweight, the number of overweight and obese mothers is increasing as well. This represents a serious problem in health care, as there are numerous health and birth problems known to be associated with obesity in pregnancy. These problems include but are not limited to: increased risk of miscarriage, birth trauma, protracted labor, hemorrhage, congenital malformations, hypertension, gestational diabetes, preeclampsia, anesthetic

complications, vaginal birth after cesarean (VBAC) failure, instrumental delivery, macrosomia, and maternal death. [3, 4] In an effort to combat obesity, many women are electing to undergo various interventions such as diet and exercise or even surgery; however, some of these interventions in women of a reproductive age who are initiating pregnancy may have consequences on birth outcomes. The focus of this paper will be to conduct a systematic review of the effects of pre-pregnancy weight loss on perinatal outcomes among overweight and obese mothers.

Historical Perspective of Obesity

Obesity is defined by the World Health Organization (WHO) as abnormal or excessive fat accumulation that may impair health. The National Institute of Health's (NIH) definition of overweight and obesity is based on a person's Body Mass Index (BMI), a number obtained by combining a person's height in meters and weight in kilograms. Due to the ease with which it can be calculated and its relative accuracy in estimating the amount of a person's visceral fat, BMI has become the most widely used measure in determining categories of bodyweight. This number is generally considered to be an appropriate substitute for the actual measurement of a person's adiposity, especially on population levels. An adult with a BMI between 18.5 – 24.9 kg/m^2 is considered to be of normal weight. An adult with a BMI between 25.0 – 29.9 kg/m^2 is considered to be overweight. Obesity is described as any BMI over 30.0 kg/m^2 with further subdivisions into classes of obesity. There are three defined classes of obesity with class I being the least severe (BMI 30.0 – 34.9 kg/m^2) and classes II (35.0 – 39.9 kg/m^2) and III (≥ 40.0 kg/m^2) being successively greater in weight and severity.[3] The obesity classes aid in determining treatment options: therapeutic lifestyle changes such as increased physical activity and decreased dietary intake are indicated for all mildly obese individuals (class I), while more aggressive

forms of weight loss such as bariatric surgery or pharmacotherapy are indicated for people with more extreme obesity (class II or III).[5] These measures of BMI are illustrated in Table 1.

Table 1. Body mass index (BMI) and obesity

	BMI (kg/m^2)
Normal weight	18.5 – 24.9
Overweight	25.0 – 29.9
Obese	≥ 30.0
Class I obesity	30.0 – 34.9
Class II obesity	35.0 – 39.9
Class III obesity	≥ 40.0

The proportion of people who are obese has increased in the United States over the past 50 years, and with the spread of Western diets and the effects of globalization, the proportion of people who are obese has increased around the world.[6] In 1962, just 13% of the US population was classified as obese; today, over two-thirds of the country is either overweight or obese. Since 1980, obesity rates in adults has doubled and children aged 12-19 have tripled their obesity rates.[3] Obesity has become a chronic health risk, contributing to greater than 100,000 deaths per year, and it has been recognized as a leading cause of premature mortality in women in the US.[7]

Causes of Obesity

While the primary cause of While the primary cause of obesity is thought to be a "multifactorial milieu" of environmental, behavioral, genetic, and socioeconomic factors[3], more concrete reasons for the recent obesity epidemic can be attributed to the rise in the availability and consumption of energy-dense foods in conjunction with the lack of physical activity by modern society. Other factors associated with the rise in obesity include an increase in sleep debt, endocrine disrupting chemicals,

pharmaceutical iatrogenesis, as well as a reduction in the variability of ambient temperatures. Although the aforementioned factors affect both men and women, there is a specific factor contributing to the obesity epidemic which is exclusive to women: pregnancy. Both epigenetic and non-epigenetic factors in pregnant women have been shown to contribute to the obesity of offspring. There is growing evidence that maternal obesity can epigenetically impact offspring through intrauterine effects. Additionally, the phenomenon of increasing maternal age in modern societies has been connected to increased obesity in children.[6]

Obesity and Pregnancy

While pregnancy has been shown to affect obesity in offspring, the obesity epidemic has affected pregnancy as well. Now, more than 40% of women who are initiating pregnancy are overweight or obese. Eight percent of these pregnant women are classified as class III obese, with a BMI of ≥ 40.0 kg/m^2.[3] These kinds of excessive weight gain and obesity during pregnancy have been identified as independent risk factors for maternal and fetal complications of pregnancy, often with significant lifelong consequences.[7] This fact is concerning because greater than 60% of previous gravidas, women who have given birth previously, become overweight or obese with their subsequent pregnancies. The compounded effects of obesity in multiparous women can adversely affect the gestational environment of the fetus.[39] Artal et al propose that excessive weight gain during pregnancy can cause an intergenerational "vicious cycle" of obesity, causing overweight or obese mothers to give birth to macrosomic daughters, who are then likely to become obese and give birth to macrosomic offspring themselves.[7]

Although it has been clearly established that obesity has a negative impact on women and in particular, women who are pregnant or initiating pregnancy, the impact on birth outcomes of obese women who

are trying to lose weight prior to pregnancy is less clear. While there is much research and literature available on the management of obese women during pregnancy and the maternal outcomes associated with obesity, many of these studies do not discuss the effects of weight loss in obese women on birth outcomes. Much of the research that has been conducted is very dated and does not have specific recommendations for the various classes of obesity or the impact on birth outcomes. For example, the Institute of Medicine (IOM) determined in 2009 that overweight women (BMI 25.0 – 29.9) should limit their gestational weight gain (GWG) to 7-11.5 kg, while obese women (BMI ≥ 30) should limit their GWG to 5-9 kg, compared to the suggested GWG of 11.5-16 kg for women of normal weight (BMI 18.5-24.9). These recommendations from the IOM were based on evidence from studies such as Kiel et al. and Bodnar,et al. that state that limits to weight gain in morbidly obese women may be beneficial for birth outcomes.[8, 9] However, the IOM was not able to provide specific recommendations for the three classes of obesity due to lack of research.[10] Recently published research suggests that moderate weight gain, rather than weight loss, is most appropriate for obese mothers, but that the amount of suggested weight gain should be tailored for mothers depending on their class of obesity.[11]

Obesity and Birth Outcomes

A main focus of this paper will be trying to discern the impact on birth outcomes in overweight or obese women with pre-pregnancy weight loss. In trying to ascertain the effects of overweight and obesity on birth outcomes, it is important to separate them from the effects of pre-existing conditions such as diabetes. This is difficult, as most studies that study obesity and weight loss will include a significant number of women with hyperglycemia. Furthermore, controversy has long existed as to whether the adverse effects of overweight/obesity and hyperglycemia associated with birth outcomes are independent.[6] Early studies of nulliparous women proposed that hyperglycemia and obesity were not independent risk factors for macrosomia and hypertensive disorder in pregnancy, and that hyperglycemia was more significantly related to adverse outcomes.[34] In contrast, other studies that looked at women with gestational diabetes came to the conclusion that maternal obesity was the stronger risk factor for macrosomia.[35] To further confound things, several other studies that observed women with and without gestational diabetes suggested that obesity was associated with higher rates of hypertension and macrosomia, but that gestational hyperglycemia was associated with cesarean section. Larger, more recent studies in the US and Spain have demonstrated an independent, increased risk of cesarean section and macrosomia with maternal obesity, pre-existing diabetes, diet-treated gestational diabetes, and insulin-treated gestational diabetes.[36 37 38] Together, these studies suggest that maternal obesity and maternal hyperglycemia do have an independent impact on several of the birth outcomes listed above.[6]

Obesity Interventions

Clearly, as we begin to understand the adverse effects that overweight and obesity have on all aspects of health, the importance of weight loss and weight loss interventions becomes paramount. Interventions for the management of obesity have been broadly described as fitting into three categories: behavioral, medical, and surgical.

Behavioral Interventions

Behavioral weight loss interventions include diet and exercise. These interventions are difficult for patients to sustain on a long-term basis and require considerable support and motivation. Considerable weight loss can occur but can be easily regained if there is not strict adherence to the behavioral change.[12]

Medical Interventions

Medical interventions usually consist of weight loss medications used in conjunction with diet and exercise such as orlistat, sympathomimetic drugs, and other commonly used over-the-counter pharmaceuticals. Many of these medications have adverse side effects due to their mechanism of action. Orlistat, for example, is a lipase inhibitor that reduces digestion and absorption of dietary fat. Sympathomimetic drugs such as phentermine or diethylpropion are drugs that are used for short term weight loss. They are amphetamine derived antisuppressants that centrally release dopamine and noradrenaline.[13] A systematic review by Neovius et al. showed that pharmacologic therapy can be an effective method to achieve significant weight loss.[14]

Surgical Interventions

Surgical procedures for weight loss are encompassed in the field of bariatric surgery. This has been shown to be the most effective method for long-term substantial weight loss; thus it is very effective at improving or relieving obesity-related comorbidities, increasing quality of life, and decreasing mortality. Bariatric surgery can be further classified into two sub-categories: restrictive procedures and malabsorptive procedures. Restrictive procedures limit the volume of food the stomach can hold and slow its release into the intestines. Today, the most commonly performed restrictive procedure is adjustable gastric banding. In contrast, malabsorptive procedures restrict the absorption of nutrients to the terminal ileum, where food and digestive enzymes are finally able to mix. Currently, this type of procedure is only considered for individuals with a BMI greater than 50, as problems with protein malnutrition, micronutrient deficiencies, and diarrhea are common.[12]

Another surgical intervention, the Roux-en-Y gastric bypass, is a hybrid restrictive/malabsorptive procedure now frequently performed laparoscopically. In this procedure the stomach is divided into "a small proximal pouch and a distal bypassed remnant. The proximal jejunum is anastomosed with this pouch to form the gastric limb, whereas the end of the duodenum is anastomosed with the distal jejunum to form the biliary limb. The remaining small bowel distal to the duodenal anastomosis forms a common limb where food finally mixes with pancreatic and biliary secretions, with the result that nutrients can be absorbed."[12]

Together, Roux-en-Y gastric bypass and laparoscopically-placed adjustable gastric banding (LAGB) are the most commonly performed surgical weight loss procedures. The National Institute for Health and Clinical Excellence (NICE) guidelines recommend bariatric surgery as a weight loss treatment option only for those with a BMI >40 or those with a BMI >35 with significant comorbidities that could be improved

with weight loss. Additionally, patients must have failed to achieve or sustain adequate weight loss for a period of at least 6 months using all non-surgical methods, and should be receiving or be due to receive intensive management in a specialist obesity service. They must also be physically fit for surgery and able to commit to long-term follow-up care.[12]

Obesity Interventions and Pregnancy

Each of the aforementioned methods for weight loss is available for overweight and obese women of childbearing age. This paper will focus on the effects of pre-pregnancy weight loss on birth outcomes including premature delivery, macrosomia, shoulder dystocia, low birth weight, and perinatal mortality. The ideal time for intervention (weight loss) is certainly before pregnancy, as weight loss during pregnancy increases the risk of delivering an infant that is small-for-gestational age (SGA)[10]

Therefore, it is important to ascertain just how effective weight loss interventions can be for overweight and obese women attempting to have children, and how this intervention will affect the outcome of their pregnancies. Thus, we need a systematic review of the question: Among overweight and obese women of childbearing age, does pre-pregnancy weight loss lower the incidence of adverse pregnancy outcomes such premature delivery, intrauterine growth restriction, low birth weight, macrosomia, shoulder dystocia, cesarean section, preeclampsia, and perinatal mortality?

Methods

The focused question that this paper will address is: "Among overweight and obese women of childbearing age, does pre-pregnancy weight loss lower the incidence of adverse pregnancy outcomes such as premature delivery, intrauterine growth restriction, low birth weight, macrosomia, cesarean section, preeclampsia, and perinatal mortality?" For the purposes of this systematic review, premature delivery is defined as birth before 37 weeks of gestation. Intrauterine growth restriction (IUGR) is defined as a fetus whose weight is below the 10th percentile for its gestational age. Low birth weight is defined as a newborn infant weighing less than 2500 grams at birth. Macrosomia is defined as a newborn infant weighing greater than 4000 grams at birth.

Table 2. Clinical question in PICOTS format

PICOTS Clinical Question Table	
Patient/Problem	Overweight and obese women of childbearing age (BMI >25)
Intervention	Weight loss via traditional methods (dieting, weight loss programs) or via bariatric surgery
Comparison	No weight loss
Outcome	Pregnancy outcomes: premature delivery, IUGR, low birth weight, macrosomia, cesarean section, preeclampsia, perinatal mortality
Timing	All studies after 1985
Studies	Prospective and retrospective cohort studies, Case-control studies, and RCTs

In formulating my focused question, I decided to search for literature on studies on weight loss in the pre-pregnancy or interpregnancy period. Studies looking at gestational weight management in obese and overweight mothers have already been reviewed,[11, 15] and guidelines on gestational weight gain have already been established to optimize fetal and maternal outcomes. Therefore I will not be reviewing studies about the effects of weight loss or weight management during pregnancy. This review

will also not focus on the maternal outcomes of overweight and obesity on maternal outcomes. The effects of overweight and obesity on maternal outcomes of pregnancy have also already been reviewed.[4] I will also not be looking at the effects of weight loss on conception and fertility. While this is an interesting area of research, the goal of this paper is to focus on perinatal outcomes, specifically the effects on the newborn. Studies that only attempted to compare different weight loss methods to each other and did not focus on obese or non-obese populations were not included as they do not have much utility in addressing the focused question of this paper. I also excluded case studies and studies that included less than 20 participants in the study group. Furthermore, studies that looked at birth outcomes specifically in patients with other comorbid conditions were excluded from this review. No preference was given to studies regarding birth order and number of pregnancies (gravidity and parity) of the subjects studied. I also chose not to search for articles on the downstream effects of weight loss on later outcomes in the child's life, instead choosing to focus specifically on the birth period.

Eligibility criteria

I included English language studies that stated a goal of determining the effects of weight loss on various perinatal outcomes, in a population consisting of overweight and obese women. The amount of acceptable weight loss before conception did not need to be specified a priori. No preference was given to the method of weight loss before pregnancy in selecting studies, as studies concerning weight loss in the pre-pregnancy period are scarce. Studies needed to have a defined focus on perinatal birth outcomes that affected the fetus/newborn, with data that specifically examined the effects of maternal weight loss on the fetus/newborn and the birth process. It was acceptable if the studies also examined maternal outcomes and newborn outcomes after the birth process, although these outcomes were not evaluated in this systematic review. All studies that compared outcomes between those with weight loss

intervention before pregnancy in overweight/obese women and those women without the weight loss intervention before pregnancy who were overweight/obese (BMI between 18.5 -24.9) were included.

Search Strategy

I searched PubMed for the terms "pregnancy outcomes" and "weight loss" and "obesity" in addition to another search using the terms "pregnancy outcomes" AND "maternal weight loss." These two searches returned 151 and 477 search results respectively. From these searches, a total of 10 studies were found that fulfilled the previous eligibility criteria. Noting that bariatric surgery was a frequent intervention for weight loss found in the eligible studies, I performed another PubMed search using the search terms "bariatric surgery" and "pregnancy outcomes." This returned 112 search results, of which 8 were found to fulfill criteria. I then searched the ISI Web of Knowledge database using the search terms "obesity" and "weight loss" and "pregnancy outcomes". This returned 87 search results, of which 5 were eligible. Using literature reviews found during the preceding PubMed searches, I also searched the reference lists of two other reviews. There were a total of 194 references between the two studies, of which 14 studies (7+7 studies, with some overlap) were eligible for consideration in this paper. Table 3 illustrates the specific search strategies used to obtain eligible studies. A total of 10 cohort and case-control studies were found that satisfied the previously stated eligibility criteria.

Table 3. Search strategy for finding relevant studies pertaining to clinical question

Database	Date Searched	Search Terms	Number of Results/Abstracts	Number of Studies Fitting Study Criteria*
PubMed	4/10/2011	"Pregnancy outcomes" AND "weight loss" AND "obesity"	151	4
PubMed	5/23/2011	"pregnancy outcomes" AND "maternal weight loss"	477	6
PubMed	5/22/2011	"Bariatric Surgery" AND "Pregnancy Outcomes"	112	8
ISI Web of Knowledge	5/22/2011	Obesity AND weight loss AND pregnancy outcomes	87	6
Citations from review: Maggard, et al. "Pregnancy and Fertility Following Bariatric Surgery."	5/22/2011	N/A	83	7
Citations from review: Kominiarek, MA. "Pregnancy After Bariatric Surgery."	5/22/2011	N/A	111	7

*There was overlap in studies found obtained through different search strategies

Quality Criteria

I used the USPSTF Quality Rating Criteria to evaluate each of the studies in this systematic review. The USPSTF first rates the hierarchy of research designs. It ranks the quality of well designed study types from randomized controlled trials to case studies. The hierarchy is demonstrated below in table 4.

Table 4. Hierarch of research design[16]

I	Evidence obtained from at least one properly randomized controlled trial.
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience, descriptive studies and case reports, or reports of expert committees.

The studies obtained for this systematic review consist of case-control and cohort studies. I assessed the quality of these studies by rating the internal validity of each study using three categories: "good," "fair," and "poor." The USPSTF has created a set of operational parameters for evaluating the internal validity of these designs. The criteria used to determine which of the three categories to assign to a study are demonstrated below in table 5. I assigned a rating of "good" to a study which meets all criteria, a rating of "fair" for a study that does not meet all criteria but has no flaw which invalidates its results, and a rating of "poor" to a study found to have a flaw which does invalidate its results.[16,17]

Table 5. Criteria for grading the internal validity of individual studies[16]

Study Design	Criteria
Case-control studies	• Accurate ascertainment of cases • Nonbiased selection of cases/controls with exclusion criteria applied equally to both • Response rate • Diagnostic testing procedures applied equally to each group • Appropriate attention to potential confounding variables
Cohort studies	• Initial assembly of comparable groups: consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts • Maintenance of comparable groups (includes attrition, crossovers, adherence, contamination) • Important differential loss to follow-up or overall high loss to follow-up • Measurements: equal, reliable, and valid (includes masking of outcome assessment) • Clear definition of interventions • All important outcomes considered • Analysis: adjustment for potential confounders

Table 6. Ratings of internal validity for Case-control and Cohort studies[16]

Study Design	Ratings
Case-control studies	Good: Appropriate ascertainment of cases and nonbiased selection of case and control participants; exclusion criteria applied equally to cases and controls; response rate equal to or greater than 80 percent; diagnostic procedures and measurements accurate and applied equally to cases and controls; and appropriate attention to confounding variables. Fair: Recent, relevant, without major apparent selection or diagnostic work-up bias but with response rates less than 80 percent or attention to some but not all important confounding variables. Poor: Major section or diagnostic work-up biases, response rates less than 50 percent, or inattention to confounding variables.
Cohort studies	Good: Evaluates relevant available screening tests; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner; includes large number (more than 100 broad-spectrum of patients). Fair: Evaluates relevant available screening tests; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50 to 100 subjects) and a "medium" spectrum of patients.

	Poor: Has fatal flaw such as: Uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size or very narrow selected spectrum of patients.

The external validity of each study was also determined using U.S. Preventive Services Task Force (USPSTF) criteria. Studies were rated "good" if the study differed minimally from the US primary care population/situation/providers; "fair" if the study differed from the US primary care population/situation/providers in a few ways that had the potential to affect the outcome in a clinically important way; or "poor" if the study differed from the US primary care population/situation/providers in many ways that had a high likelihood of affecting the clinical outcomes.[18] These criteria are illustrated in table 7.

Table 7. Criteria for rating external validity[18]

External validity is rated "good" if:	The study differs minimally from the US primary care population/situation/providers and only in ways that are unlikely to affect the outcome; it is highly probable (>90%) that the clinical experience with the intervention observed in the study will be attained in the US primary care setting.
External validity is rated "fair" if:	The study differs from the US primary care population/situation/providers in a few ways that have the potential to affect the outcome in a clinically important way; it is only moderately probable (50%-89%) that the clinical experience with the intervention in the study will be attained in the US primary care setting.
External validity is rated "poor" if:	The study differs from the US primary care population/ situation/ providers in many way that have a high likelihood of affecting the clinical outcomes; the probability is low (<50%) that the clinical experience with the intervention observed in the study will be attained in the US primary care setting.

Approach to finding and selecting articles

In total, I reviewed 1021 articles and abstracts, of which I thoroughly reviewed 55 full text articles. Through this process I was able to narrow the number of studies which fulfilled all eligibility criteria to 10 studies. The search strategy and abstracts subsequently underwent review by another person assisting with the search, who agreed with the results of the search.

Data Extraction

In this review, the author performed data extraction solely; later, a second person separately reviewed the data extraction forms for accuracy and completeness. For each study, the following information was extracted: general information (including date of data extraction, article title and author(s), country of origin, source of funding); study question and study objective(s); research design; source population; study population and general characteristics, eligibility (inclusion and exclusion criteria) and recruitment procedures; initial comparability of groups; number of drop outs; potential for selection bias; measurements of interventions and outcomes; description of intervention(s) and control(s); statistical techniques used and reliability and validity of measurements; whether blinding was performed; potential for measurement bias; potential confounders and overall potential for confounding; method of outcome analysis (however this is likely not an issue in the study designs being evaluated); results/outcomes; and a judgment of internal and external validity based on pre-specified USPSTF methods; secondary outcome; adverse outcomes and potential conflicts of interest. A standardized form was constructed and used to evaluate each study using these criteria.

Synthesizing Evidence

As this is a review of many non-randomized studies dealing with clinical heterogeneity of interventions as well as many different pregnancy outcomes, a complete meta-analysis and pooling of data may not be the most sensible approach at this time. The evidence abstracted from this analysis will be synthesized in a table format detailing the study title, author(s), country, funding, intervention(s) and comparison(s), inclusion and exclusion criteria, population characteristics, outcome assessment, results, analysis, attrition/loss to follow-up, adverse effects, and quality rating. An example of the table to be used is given below (Table 8). The evidence will also be described in a narrative format to fully interpret the collected data. This process will include initial standardized textual descriptions of each study included in the review. If necessary, every attempt will be made to transform the data into a common measure to allow an accurate description of the range of effects. Finally, the overall evidence profile of all studies included in this review will be performed, taking into account the number of studies/patients, study designs, overall quality of studies, consistency of studies, directness of studies in answering the clinical question, overall effect of the intervention, and the overall grade of the evidence (Table 8).

Table 8. Example data extraction table

Study	JAMA Citation: Country:
Study Question:	
Date of extraction:	
Source of Funding:	
Source Population	
Study Population:	 Exclusion criteria:
Design	Study Design: Setting: Sample size:
Intervention	
Potential for selection bias	
Population characteristics	Randomization? Groups similar at baseline?
Outcome assessment	Primary outcome measures: Preterm birth? IUGR? Low birth weight? Macrosomia? Cesarean section? Preeclampsia? Perinatal morality?
Measurement	Study Groups: Exposure measures: Outcomes: Outcome measures:
Potential for measurement bias	
Potential for confounding	
Analysis	
Results	
Adverse Effects	
Attrition	Number of dropouts?
Overall judgment of internal validity (Quality Rating)	
External validity	

Table 9. Evidence Profile Template

No. of Studies/Patients	Study Designs	Study Quality	Consistency	Directness	Overall effect of the intervention	Overall grade of the evidence

To minimize bias in interpreting results, the narrative framework established by Economic and Social Research Council (ESRC) Methods Programme for narrative synthesis in systematic reviews will be followed.

The framework consists of four elements.[19, 20]

1. Developing a theory of how the intervention works, why and for whom
2. Developing a preliminary synthesis of finding of included studies
3. Exploring relationships within and between studies
4. Assessing the robustness of the synthesis

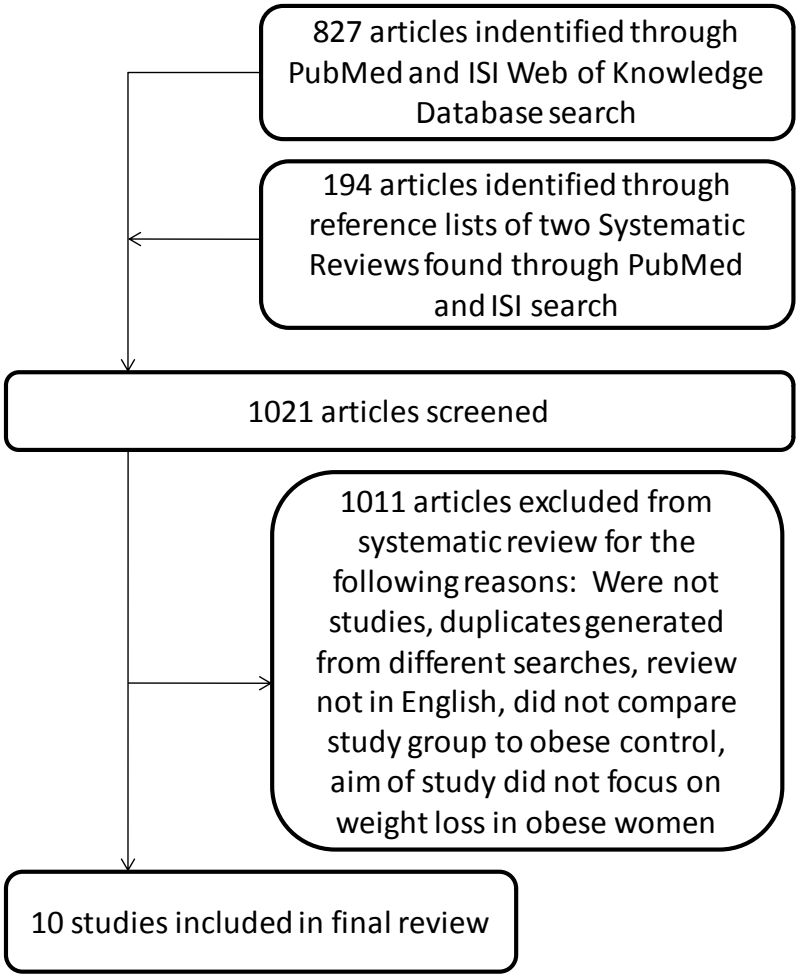
The synthesis of the evidence will take into account the different methods of weight loss amongst studies. Subgroups will be formed according to pre-intervention BMI, splitting up the data according to groupings of overweight (BMI 25.0- 29.9) and obese (BMI >30.0). The relationships within and between studies will be explored via qualitative case descriptions, using quantitative data to explain similarities and differences in study findings and to explain possible statistical outliers. At this point, more weight will be given to studies that were performed with the highest quality and technical precision according to the quality assessments performed earlier. Finally, an overall assessment on the strength of all available evidence and any conclusions that can be made will be performed.

Results

Study Selection

A total of 1021 abstracts from the literature search and reference lists were reviewed; of these, 55 full text articles were further reviewed. Ten studies met the inclusion criteria; these consisted of six case-control studies and four cohort studies. Figure 1 summarizes the flow of information through the systematic review phases and explains reasons for exclusion of articles.

Figure 1. PRISMA diagram



Studies were reviewed in alphabetical order by title. Full data extraction tables are shown in Appendix A.

Study 1

Citation	Dixon, JB; Dixon, ME; O'Brian, PE; "Birth Outcomes in Women After Laparoscopic Adjustable Gastric Banding." Obstet Gynecol 2005; 106: 965-72
Study population	All women (79) in the LAGB program who became pregnant after LABG placement.
Study Design	Retrospective case-control
Results	Lower rates of low birth wt, high birth wt., preterm birth, and preeclampsia in LAGB group, but p-value only given for preeclampsia.
Internal validity	Fair
External validity	Fair

The Dixon et al. study, "Birth Outcomes in Obese Women After Laparoscopic Adjustable Gastric Banding" is a case-control study published in Obstetrics and Gynecology in 2005. Seventy-nine women were found to have given birth after laparoscopic adjustable gastric banding (LAGB) surgery were selected from a group of 1,382 patients who had had the weight loss procedure performed between January 1, 1995, and August 31, 2003. These cases were compared to seventy-nine "severely obese" women matched for parity, maternal age, and BMI.[21]

The internal validity of the study was deemed to be "fair" based on the moderate amounts of selection bias, measurement bias, and confounding. The external validity was deemed to be fair as the weight loss intervention studied is usually only performed on very obese individuals. The study demonstrated that the women who gave birth post-LAGB had lower rates of low birth weight (6.3% compared to 8.9%), high birth weight (11.4% compared to 17.7%), preterm birth (6.3% compared to 12.7%), and

preeclampsia (5% compared to 25%). No p-values were given for low birth rate, high birth rate, or preterm birth, but preeclampsia was significant with p <0.05.

Study 2

Citation	Weintraub, AY.; Levy, A; Levi, I; Mazor, M; Wiznitzer, A; Sheriner, E. "Effect of bariatric surgery on pregnancy outcome." International Journal of Gynecology and Obstetrics, 2008, 103, 3, 246
Study population	301 deliveries preceding bariatric surgery and 507 deliveries following bariatric surgery.
Study Design	Retrospective cohort
Results	Higher rates of IUGR, low birth weight, and cesarean section in bariatric surgery group. Lower rates of severe preeclampsia, perinatal mortality, macrosomia. Only rates cesarean section, severe preeclampsia, and macrosomia were found to be significantly different.
Internal validity	Good
External validity	Fair

The Weintraub et al. study "Effect of Bariatric surgery on pregnancy outcome" is a retrospective cohort study that compared the perinatal outcomes of women who delivered before with women who delivered after bariatric surgery in a tertiary medical center between 1988 and 2006. Data used was from 176 women that had 301 deliveries before bariatric surgery and 354 women who had 507 deliveries after bariatric surgery.[22] While pregnancies following bariatric surgery were characterized by advanced maternal age and greater parity and gravidity, these factors and other potential confounder were controlled for through a multivariate logistic regression model.

The internal validity of the study was deemed "good" as there were low levels of selection bias, measurement bias, and confounding. The external validity of the study was deemed fair, as the study population was fairly homogenous and the method of weight loss is recommended only for very obese

women. This study demonstrated that women who delivered after bariatric surgery had lower rates of macrosomia (3.2% compared to 7.6%; p = 0.004) and perinatal mortality (1.0 compared to 2.3%; p = 0.11). However they also had higher rates of IUGR (3.9% compared to 2.3%; p = 0.15), cesarean section (30.0% compared to 17.9%; p <0.0001), and low birth weight (11.8% compared to 9.0%; p = 0.12).

Study 3

Citation	Deitel, M.; Stone, E.; Kassam, H.A.; Wilk, E.J.; Sutherland, D.J.A. "Gynecologic-Obstetric Changes after Loss of Massive Excess Weight following Bariatric Surgery" J. Am. Coll. Nutr. 7: 147, 1988.
Study population	15 pregnancies following bariatric surgery (three types:
Study Design	Prospective cohort
Results	Higher rate of perinatal mortality (spontaneous abortion) in the post-bariatric surgery group, but lower rates of cesarean section and preeclampsia.
Internal validity	Poor
External validity	Poor

The Dietel et al. study "Gynecologic-Obstetric Changes after Loss of Massive Excess Weight following Bariatric Surgery is a prospective cohort study that compared obstetric features of nine women (sixteen pregnancies) after bariatric surgery to eighty-six women who had pregnancies before bariatric surgery. This study was performed in 1988, and was only two pages long.[23]

The internal validity of the study was deemed "poor" due to high levels of selection bias, measurement bias, and confounding. The external validity of the study was also deemed "poor" due to the age of the study. The study showed a higher rate of spontaneous abortions in the post-bariatric surgery group

(40% compared to 25.2%; no p-value given), but lower rates of cesarean section (0% compared to 25.2%; no p-value given) and preeclampsia (0% compared to 12.8%; p <0.001).

Study 4

Citation	Skull, A.J.; Slater, G.H.; Duncombe, J.E.; Fielding, G.A. "Laparoscopic Adjustable Banding in Pregnancy: Safety, Patient Tolerance and Effect on Obesity-Related Pregnancy Outcomes" Obesity Surgery, 14, 230-235.
Study population	44 women
Study Design	Retrospective case-control
Results	LAGB group had lower rate of preeclampsia, but higher rates of elective cesarean section, emergency cesarean section.
Internal validity	Poor
External validity	Fair

The Skull et al. study "Laparoscopic Adjustable Banding in Pregnancy: Safety, Patient Tolerance and Effect on Obesity-Related Pregnancy Outcomes" is a retrospective case-control study comparing outcomes of laparoscopic adjustable gastric banding (LAGB) pregnancies with previous non-LAGB pregnancies. A total of forty-nine LAGB pregnancies were compared to a historical control of thirty-one previous non-LAGB pregnancies.[24]

The study stated: "For outcomes where confounding could be responsible for the outcome rather than LAGB, multiple regression was used." The internal validity of the study was deemed "poor" due to a high potential of selection bias and measurement bias as well as moderate potential for confounding. The external validity of the study was deemed "fair." The study demonstrated that women who had LAGB pregnancies had lower rates of preeclampsia (0% compared to 6.4%; p = 0.06). However they had

higher rates of elective cesarean section (24.5% compared to 9.5%; p = 0.10), and emergency cesarean section (4% compared to 3.2%; p = 0.10).

Study 5

Citation	Ducarme, G.; Revaux, A.; Rodrigues, A.; Aissaoui, F.; Pharisien, I.; Uzan, M. "Obstetric outcome following laparoscopic adjustable gastric banding." International Journal of Gynecology and Obstetrics (2007) 28, 244-247.
Study population	13 obese women who had undergone LAGB were the study cases, 414 obese women who had not served as controls
Study Design	Retrospective case-control study
Results	Slightly higher rate of preterm birth, but lower rates of low birth weight, macrosomia, cesarean section, preeclampsia in LAGB group.
Internal validity	Fair
External validity	Fair

The Ducarme et al. study "Obstetric outcome following laparoscopic adjustable gastric banding" is a retrospective case-control study comparing the obstetric outcomes of thirteen obese women who underwent LAGB with four hundred and fourteen obese women who did not undergo surgery.[25]

The internal validity of the study was deemed "fair" as there was a moderate potential for selection bias, low to moderate potential for measurement bias, and moderate to high potential for confounding. The external validity of the study was deemed "fair" as the LAGB procedure is recommended only for very obese women. The study demonstrated that the while the LAGB pregnancy group had a slightly higher rate of preterm birth than the obese non-LAGB group (7.7% compared to 7.1%; not significant), the LAGB group also had lower rates of low birth weight (7.7% compared to 10.6%; p<0.05), macrosomia

(7.7% compared to 14.6%; p<0.05), cesarean section (15.3% compared to 34.4%; p<0.01), preeclampsia (0% compared to 3.1%; p<0.05).

Study 6

Citation	Marceau, P.; Kaufman, D.; Biron, S.; Hould, F.; Lebel, S.; Marceau, S.; Kral, J.G. "Outcome of Pregnancies after Biliopancreatic Diversion." Obesity Surgery, 14, 2004; 318-324.
Study population	132 women gave birth post-BPD resulting in 251 postoperative pregnancies
Study Design	Retrospective case-control study
Results	Slightly higher rate of preterm birth in BPD group, but lower rates of low birth weight, macrosomia, cesarean section, preeclampsia.
Internal validity	Poor
External validity	Fair

The Marceau et al. study "Outcome of Pregnancies after Biliopancreatic Diversion" is a retrospective cohort study performed in 2004. The authors investigated the obstetric outcomes before and after biliopancreatic diversion (BPD) in women who have undergone the procedure due to morbid obesity. The study compared 251 post-BPD pregnancies to 1,577 pre-BPD pregnancies in the same group of women.[26]

The internal validity of the study was deemed "poor" due to the moderate to high potential for selection bias and the high potential for measurement bias and confounding. The external validity of the study was deemed "fair" as the study did investigate a procedure indicated only for very obese women, but also included a large number of women who were likely representative of the population.

The study demonstrated that post-BPD pregnancy group had higher rates of low birth weight (9.6% compared to 3.1%) and miscarriages (26% compared to 21.6%) when compared to the pre-BPD obese control group. However, the post-BPD pregnancy group was also found to have lower rates preterm birth (13.6% compared to 16.7%), macrosomia (7.7% compared to 34.8%), and stillbirths (0.6% compared to 1%). P-values were not given for any of these outcomes, so the significance of these differences is unknown.

Study 7

Citation	Wittgrove, A.C.; Jester, L.; Wittgrove, P.; Clark, G.W. "Pregnancy Following Gastric Bypass for Morbid Obesity" Obesity Surgery (1998), 8, 461-464.
Study population	36 patients who had undergone RYGB and had singleton pregnancies after the procedure
Study Design	Retrospective case control
Results	Slight higher rate of preterm birth and cesarean section in gastric bypass group, but lower rate of macrosomia.
Internal validity	Poor
External validity	Fair

The Wittgrove et al. study "Pregnancy Following Gastric Bypass for Morbid Obesity" is a retrospective case-control study performed in 1998. The authors aim was to investigate "the risks and complications after gastric bypass surgery" by comparing the pregnancy outcomes of 36 women in the patient population who had given birth after Roux-en-Y gastric bypass (RYGB) procedures to the pregnancy outcomes of 17 of the same women who had given birth pre-RYGB.[27] Information was gathered via questionnaire, personal interview, and review of perinatal records.

The internal validity of the study was deemed "poor" due to a high potential for selection bias, a low to moderate potential for measurement bias, and a high potential for confounding. The external validity of the study was deemed "fair" as the study did investigate a procedure indicated only for very obese women, but was also performed in the US and used a widely performed bariatric procedure.

The study demonstrated that the post-RYGB group had a slightly higher ratio of pregnancies resulting in cesarean section (13/36 babies compared to 6/17 babies, or 36.1% compared to 35.3%) when compared to the pre-RYGB group. However, the post-RYGB group was also found to have a lower ratio of pregnancies resulting in preterm birth (4/36 compared to 3/23, or 11.1% compared to 13.0%) and macrosomia (2/36 babies compared to 7/23 babies, or 5.5% compared to 30.4%).

Study 8

Citation	Patel, J.A.; Patel, N.A.; Thomas, R.L.; Nelms, J.K.; Colella, J.J. "Pregnancy outcomes after laparoscopic Roux-en-Y gastric bypass" Surgery for Obesity and Related Diseases ,4 (2008), 39-45.
Study population	26 patients who delivered after LRYGB and 254 controls
Study Design	Retrospective case-control
Results	Higher rates of preterm birth, low birth weight, and primary cesarean section compared to obese controls, but lower rates of preeclampsia and macrosomia. Neither group had any patients experiencing perinatal mortality (stillbirth and spontaneous abortion).
Internal validity	Good
External validity	Good

The Patel et al. study "Pregnancy outcomes after laparoscopic Roux-en-Y gastric bypass" is a retrospective case-control study performed in 2008. The goal of the study was to investigate the safety of pregnancies after laparoscopic Roux-en-Y gastric bypass (LRYGB) and its potential effect on obesity-

related perinatal complications. The outcomes of twenty-six female patients who delivered after LRYGB were compared to the outcomes of 254 controls.[28]

The internal validity of the study was deemed "good" due to the low potential for selection bias and measurement bias, and the low to moderate potential for confounding. The external validity of the study was deemed "good" as the study was performed analyzing the most common form of bariatric surgery performed in the US and was performed in a community-based, academic, tertiary care center in the US.

The study demonstrated the women who gave birth after LRYGB surgery had a higher rate of cesarean section (62.5% compared to 0%; no p-value given), preterm birth (26.9% compared to 17.9%; $p = 0.390$), and low birth weight (11.5% compared to 2.6%; $p = 0.140$) when compared to obese controls. However, women who gave birth after LRYGB had lower rates of macrosomia (0% compared to 7.7%; $p = 0.147$) and preeclampsia (3.8% compared to 7.7%; $p = 0.527$). Neither group had any stillbirths/spontaneous abortions. No p-values of any outcomes were significant.

Study 9

Citation	Hoff, G.L.; Cai, J.; Okah, F.A.; Dew, P.C. "Pre-Pregnancy Overweight Status between Successive Pregnancies and Pregnancy Outcomes" J. Women;s Health, 2009, 18, 9, 1413-17.
Study population	1,035 nulliparous women whose pre-pregnancy BMI (25.0-29.9) classified them as overweight.
Study Design	Retrospective cohort
Results	Higher rate of preterm birth but lower rate of cesarean section in weight loss group.
Internal validity	Good
External validity	Good

The Hoff et al. study "Pre-Pregnancy Overweight Status between Successive Pregnancies and Pregnancy Outcomes" was a retrospective cohort study in 2009 which investigated pregnancy and newborn outcomes associated with changes in pre-pregnancy BMI. The study used birth certificates from 1995-2004 for resident of Kansas City, Missouri, to obtain data for 1,035 overweight women. The outcomes of the second pregnancies were compared for women who had either maintained overweight status, lost weight to become normal/underweight, or gained weight to become obese.[29]

The internal validity of the study was deemed to be "good" due to the minimal potential for selection bias, measurement bias, and confounding. The external validity of the study was deemed "good" due to the large number of women sampled and the fact that a specific weight loss intervention was not investigated.

The study demonstrated that women who lost weight before their second pregnancy had a lower rate of emergency cesarean section (2.5% compared to 2.4%; $p<0.02$), but a higher rate of premature birth (5.6% compared to 8.6%; $p>0.05$).

Study 10

Citation	Mostello, D.; Chang, J.J.; Allen, J.; Luehr, L.; Shyken, J.; Leet, T. "Recurrent Preeclampsia: The Effect of Weight Change Between Pregnancies" Obstetrics and Gynecology, 2010, 116, 3, 667-672.
Study population	17,733 women whose first pregnancies were complicated by preeclampsia
Study Design	Retrospective cohort
Results	Lower rate of preeclampsia in women who lose weight between pregnancies.
Internal validity	Good
External validity	Good

The Mostello et al. study "Recurrent Preeclampsia: The Effect of Weight Change Between Pregnancies" was a retrospective cohort study performed in 2010. The authors used "maternally linked birth certificates" from 17,773 women in Missouri and divided the women into three groups: women who decreased their BMI, women who maintained their BMI, and women who increased their BMI.[30]

The internal validity of the study was deemed "good" due to low to moderate potential for selection bias, moderate potential for measurement bias, and low potential for confounding. The internal validity of the study was deemed "good" due to the large number of women included in the study as well as the decision to not focus on a particular weight loss method.

The study demonstrated that the women who decreased their BMIs had a lower rate of preeclampsia (12.8%) compared to women who maintained their BMIs (14.8%). The risk ratio of women who decreased their BMIs was 0.70 (95%CI 0.61-0.81).

Synthesis of the Evidence

Table. Single Summary Evidence Table

Study #	Citation	Study Design (n)	Internal Validity	External Validity	Results	Comments
1	Dixon, JB; Dixon, ME; O'Brian, PE; "Birth Outcomes in Women After Laparoscopic Adjustable Gastric Banding." Obstet Gynecol 2005; 106: 965-72	Retrospective case-control (79)	Fair	Fair	Lower rates of low birth wt, high birth wt., preterm birth, and preeclampsia in LAGB group, but p-value only given for preeclampsia.	Small number of cases limits the power of the study.
2	Weintraub, AY.; Levy, A; Levi, I; Mazor, M; Wiznitzer, A; Sheriner, E. "Effect of bariatric surgery on pregnancy outcome." International Journal of Gynecology and Obstetrics, 2008, 103, 3, 246	Retrospective cohort (301)	Good	Fair	Higher rates of IUGR, low birth weight, and cesarean section in bariatric surgery group. Lower rates of severe preeclampsia, perinatal mortality, macrosomia. Only rates cesarean section, severe preeclampsia, and macrosomia were found to be significantly different.	Well designed study performed in Israel.
3	Deitel, M.; Stone, E.; Kassam, H.A.; Wilk, E.J.; Sutherland, D.J.A. "Gynecologic-Obstetric Changes after Loss of Massive Excess Weight following Bariatric Surgery" J. Am. Coll. Nutr. 7: 147, 1988.	Prospective cohort (15)	Poor	Poor	Higher rate of perinatal mortality (spontaneous abortion) in the post-bariatric surgery group, but lower rates of cesarean section and preeclampsia.	This study was performed in 1988 and provided minimal information in two pages. The weaknesses of this study makes the results difficult to apply to other populations. Small number of cases.
4	Skull, A.J.; Slater, G.H.; Duncombe, J.E.; Fielding, G.A. "Laparoscopic Adjustable Banding in Pregnancy: Safety, Patient Tolerance and Effect on Obesity-Related Pregnancy Outcomes" Obesity Surgery, 14, 230-235	Case-control (80)	Poor	Fair	LAGB group had lower rate of preeclampsia, but higher rates of elective cesarean section, emergency cesarean section.	The weaknesses of this study makes the results difficult to apply to other populations.
5	Ducarme, G.; Revaux, A.; Rodrigues, A.; Aissaoui, F.; Pharisien, I.; Uzan, M. " Obstetric outcome following laparoscopic adjustable gastric banding." International Journal of Gynecology and Obstetrics (2007) 28, 244-247.	Retrospective case-control (13)	Fair	Fair	Slightly higher rate of preterm birth, but lower rates of low birth weight, macrosomia, cesarean section, preeclampsia in LAGB group.	Small nunber of cases limits power of study.
6	Marceau, P.; Kaufman, D.; Biron, S.; Hould, F.; Lebel, S.; Marceau, S.; Kral, J.G. "Outcome of Pregnancies after Biliopancreatic Diversion." Obesity Surgery, 14. 318-324.	Retrospective case-control (251)	Poor	Fair	Slightly higher rate of preterm birth in BPD group, but lower rates of low birth weight, macrosomia, cesarean section, preeclampsia.	The weaknesses of this study makes the results difficult to apply to other populations.
7	Wittgrove, A.C.; Jester, L.; Wittgrove, P.; Clark, G.W. "Pregnancy Following Gastric Bypass for Morbid Obesity" Obesity Surgery, 8, 461-464	Retrospective case-control (46)	Poor	Fair	Slight higher rate of preterm birth and cesarean section in gastric bypass group, but lower rate of macrosomia.	No p-values calculated for any outcomes. No correction for potential confounders.
8	Patel, J.A.; Patel, N.A.; Thonmas, R.L.; Nelms, J.K.; Colella, J.J. "Pregnancy outcomes after laparoscopic Roux-en-Y gastric bypass" Surgery for Obesity and Related Diseases ,4 (2008), 39-45.	Retrospective case-control (26)	Good	Good	Higher rates of preterm birth, low birth weight, and primary cesarean section compared to obese and morbidly obese controls, but lower rates of preeclampsia, IUGR, macrosomia, and perinatal mortality (stillbirth and spontaneous abortion).	While this was a quality study, no p-values were significant for any outcome investigated in the study.
9	Hoff, G.L.; Cai, J.; Okah, F.A.; Dew, P.C. "Pre-Pregnancy Overweight Status between Successive Pregnancies and Pregnancy Outcomes" J. Women;s Health, 2009, 18, 9, 1413-17.	Retrospective cohort (1,035)	Good	Good	Higher rate of preterm birth but lower rate of cesarean section in weight loss group.	Lower rate of cesarean section was significant (p<0.02), but the difference was minimal (2.4% compared to 2.5%). The difference in premature birth was not significant, but was higher rate in women who decreased BMI.
10	Mostello, D.; Chang, J.J.; Allen, J.; Luehr, L.; Shyken, J.; Leet, T. "Recurrent Preeclampsia: The Effect of Weight Change Between Pregnancies" Obstetrics and Gynecology, 2010, 116, 3, 667-672.	Population-based, retrospective cohort (17,733)	Good	Good	Lower rate of preeclampsia in women who lose weight between pregnancies.	Women who decrease BMIs have a RR of 0.70 (95% CI 0.60-0.81).

Four of ten studies had an internal validity deemed "good" after critical appraisal and data extraction. However, one of these studies, study 8 (Patel et al.) did not have any statistically significant outcomes with p-values > 0.05. These studies do appear to demonstrate that weight loss before pregnancy may be associated with lower rates of macrosomia and preeclampsia. However, weight loss surgery might also be a risk factor for the need to perform cesarean section during delivery. These findings are further supported by data from the two studies that were deemed to have "good" internal validity. These studies also found that weight loss before pregnancy was associated with lower rate of preeclampsia and macrosomia. The results from studies that were deemed to have a "poor" internal validity are likely not strong enough from which to draw any significant conclusions.

Some studies had differing results. While all "good" studies that investigated cesarean sections demonstrated that there was a higher rate of cesarean section associated with pre-pregnancy weight loss, one "fair" study demonstrated that pre-pregnancy weight loss was associated with a lower rate of cesarean section. Many studies suggested that weight loss via bariatric surgery might also be associated with higher rates of low birth weight.

Discussion

Interpretation of the evidence

The purpose of this systematic review was to determine the effects of pre-pregnancy weight loss in obese and overweight women on perinatal outcomes. However, the evidence accumulated after extracting data from the studies presents a mixed picture. The majority of studies found investigated the effects of bariatric surgery on pregnancy outcomes in morbidly obese women. While many of these studies demonstrate that weight loss secondary to bariatric surgery before pregnancy is associated with lower rates of macrosomia[22, 25, 28] and preeclampsia,[21, 25, 28]there is some discordance with respect to other perinatal outcomes.

Cesarean section

Some of the studies reviewed demonstrated that pre-pregnancy weight loss after bariatric surgery may be associated with higher rates of cesarean section,[22, 25, 28] while another study showed that prepregancy weight loss following bariatric surgery was associated with a lower rate cesarean section. Additionally, the Hoff et al. study which investigated the effects of weight loss not due to bariatric surgery on perinatal outcomes demonstrated a slightly lower rate of emergency cesarean section after weight loss.[29]

Given this evidence, it is difficult to elucidate whether the need for cesarean section is higher in all patients undergoing weight loss, or if it is in some way associated with previous bariatric surgery. Indications for cesarean section are likely to vary across institution and physician preference,[31] and there is also evidence that more women are requesting to have cesarean sections in the absence of clinical indications, making this measure even more difficult to assess.[32]

Low Birth Weight

The effects of pre-pregnancy weight loss on low birth weight was also difficult to ascertain from the evidence. The Ducarme et al. study demonstrated that bariatric surgery before pregnancy lowered the rate of low birth weight. However, other studies[22, 28] demonstrated the opposite effect, although the difference was not statistically significant in these two studies. Thus the effect of pre-pregnancy weight loss on low birth weight is unclear based on the available evidence.

Preterm birth

Only one study was found to investigate the effects of pre-pregnancy weight loss in overweight populations,[29] and it demonstrated that weight loss in this population may be associated with lower rates of premature birth, although this finding was not statistically significant. Other studies investigating the effects of weight loss from bariatric surgery on preterm birth suggest that weight loss may be associated with higher rates of preterm birth, however none of these were statistically significant.[25, 33] Thus, the effect of pre-pregnancy weight loss on preterm birth is unclear based on the available evidence.

IUGR and perinatal mortality

Only one study with an internal validity deemed "good" or "fair" by USPSTF guidelines investigated the effects of pre-pregnancy weight loss on the incidence of IUGR. The study found that there was a higher incidence of IUGR associated with pre-pregnancy weight loss due to bariatric surgery, although the difference was not found to be statistically significant.[25] Only one study with an internal validity deemed "good" or "fair" by the USPSTF guidelines investigated the effects of weight loss on perinatal mortality. While it did demonstrate that weight loss after bariatric surgery was associated with lower perinatal mortality, this result was also not significant.[22] Based on the evidence available, the association between pre-pregnancy weight loss with IUGR and perinatal mortality is unclear.

Preeclampsia

All studies investigating the effects of pre-pregnancy weight loss on preeclampsia demonstrated that weight loss was associated with a lower rate of preeclampsia.[21, 25, 28, 30] All but one study[28] showed statistical significance. This demonstrates that there may be an association with pre-pregnancy weight loss and a decrease in the rate of preeclampsia.

Limitations of the review

One of the possible limitations of this systematic review is publication bias. It is possible that I was not able to include other studies that may have fit my inclusion and exclusion criteria because they were not published. The possibility of publication bias cannot be ruled out. Sample size was also an issue. Four of ten studies reviewed had fewer than 100 cases, limiting the power of the studies. Randomized control trial are clearly not feasible options for addressing this focused question, therefore the cohort and case-control studies available represent the best available evidence at this time. The lack of high quality, well-

designed studies addressing pre-pregnancy weight loss makes the focused question of this systematic review difficult to answer.

Overall grade of evidence: Poor; the evidence is insufficient to make significant conclusions about perinatal outcomes.

Future directions

In order to adequately address the focused question of this systematic review, more well-designed studies are clearly needed. An ideal study might be a retrospective cohort design that uses birth certificate information including perinatal outcomes to determine the effects of weight loss between consecutive births in women over a period of time. If done properly, a study of this design could obtain several thousand cases and compare the perinatal outcomes of women who decreased BMI prior to second pregnancies to women who maintained or increased BMI. Such a study should be sufficiently powered to detect possible significant differences in perinatal outcomes. Additionally, the study might be able to exclude women with diabetes, allowing the results of the study to reflect the effects of weight loss only. More research is also needed to delineate some of the adverse perinatal outcomes possibly secondary to weight loss due to bariatric surgery as opposed to weight loss due to behavioral modifications.

While the health benefits of normal weight are widely known, if a decrease in pre-pregnancy BMI in obese and overweight women was discovered to have a direct association with a decrease in perinatal outcomes, perhaps a significant shift in the attitudes towards weight control during the reproductive period of a woman's life could be achieved. In terms of overall health, this may allow pregnancy and the reproductive period to be a significant time to implement positive life changes in overweight and obese

women, theoretically improving the health of women regardless of pregnancy status. At the very least, this systematic review stresses the importance of informing the public of the possible risks associated with obesity and pregnancy.

REFERENCES

1. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999-2008. *JAMA : The Journal of the American Medical Association*. 2010;303(3):235-241.

2. Wang YY. Will all americans become overweight or obese? estimating the progression and cost of the US obesity epidemic. *Obesity (Silver Spring, Md.)*. 2008;16(10):2323-2330.

3. Gunatilake RP, Perlow JH. Obesity and pregnancy: Clinical management of the obese gravida. *Am J Obstet Gynecol*. 2011;204(2):106-119.

4. Birdsall KM, Vyas S, Khazaezadeh N, Oteng-Ntim E. Maternal obesity: A review of interventions. *International Journal of Clinical Practice (Esher)*. 2009;63(3):494-507.

5. Katzmarzyk PT, Mason C. Prevalence of class I, II and III obesity in canada. *CMAJ.Canadian Medical Association journal*. 2006;174(2):156-157.

6. Simmons D. Diabetes and obesity in pregnancy. *Best Pract Res Clin Obstet Gynaecol*. 2011;25(1):25-36.

7. Artal R, Lockwood CJ, Brown HL. Weight gain recommendations in pregnancy and the obesity epidemic. *Obstet Gynecol*. 2010;115(1):152-155.

8. Bodnar LM, Siega-Riz AM, Simhan HN, Himes KP, Abrams B. Severe obesity, gestational weight gain, and adverse birth outcomes. *Am J Clin Nutr*. 2010;91(6):1642-1648.

9. Kiel DW, Dodson EA, Artal R, Boehmer TK, Leet TL. Gestational weight gain and pregnancy outcomes in obese women: How much is enough? *Obstet Gynecol*. 2007;110(4):752-758.

10. Hinkle SN, Sharma AJ, Dietz PM. Gestational weight gain in obese mothers and associations with fetal growth. *Am J Clin Nutr*. 2010;92(3):644-651.

11. Beyerlein A, Schiessl B, Lack N, von Kries R. Associations of gestational weight loss with birth-related outcome: A retrospective cohort study. *BJOG*. 2011;118(1):55-61.

12. Grundy MA, Woodcock S, Attwood SE. The surgical management of obesity in young women: Consideration of the mother's and baby's health before, during, and after pregnancy. *Surg Endosc*. 2008;22(10):2107-2116.

13. Robinson JR, Niswender KD. What are the risks and the benefits of current and emerging weight-loss medications? *Current Diabetes Reports*. 2009;9(5):368-375.

14. Neovius M, Johansson K, Rossner S. Head-to-head studies evaluating efficacy of pharmaco-therapy for obesity: A systematic review and meta-analysis. *Obes Rev*. 2008;9(5):420-427.

15. Dodd JM, Robinson JS. Gestational weight loss in overweight and obese women is associated with an increased risk of small for gestational age infants. *Evidence-based Medicine (English ed.)*. 2011.

16. **U.S. preventive services task force (USPSTF) procedure manual: Appendix VII: Criteria for assessing internal validity of individual studies**.

http://www.uspreventiveservicestaskforce.org/uspstf08/methods/procmanualap7.htm.

17. Fleming C, Whitlock E, Beil Tea. **Appendix D. USPSTF quality rating criteria and hierarchy of research design [internet]**. In: ***Primary Care Screening for Abdominal Aortic Aneurysm***. Vol 2011. Evidence Syntheses, No. 35 ed. Rockville (MD): Agency for Healthcare Research and Quality (US); 2005.

18. **U.S. preventive services task force (USPSTF) procedure manual: Appendix VIII: Criteria for assessing external validity (generalizability) of individual studies**.

http://www.uspreventiveservicestaskforce.org/uspstf08/methods/procmanualap8.htm.

19. Popay J, Roberts H, Sowden A, et al. Guidance on the conduct of narrative synthesis in systematic reviews. *ESRC Research Methods Programme*. 2006.

20. Khan KS, Riet GT, Glanville J, Sowden A,J., et al. *Undertaking Systematic Reviews of Research on Effectiveness : CRD's Guidance for those Carrying Out Or Commissioning Reviews.* 2nd ed. York: NHS Centre for Reviews & Dissemination, University of York; 2008.

21. Dixon JB, Dixon ME, O'Brian PE. Birth outcomes in obese women after laparoscopic adjustable gastric banding. *Obstet Gynecol*. 2005;106(5, part 1):965-972.

22. Weintraub AY, Levy A, Levi I, Mazor M, Wiznitzer A, Sheiner E. Effect of bariatric surgery on pregnancy outcome. *International Journal of Gynecology and Obstetrics*. 2008;103(3):246.

23. Deitel M, Stone E, Kassam HA, Wilk EJ, Sutherland DJ. Gynecologic-obstetric changes after loss of massive excess weight following bariatric surgery. *Obstet Gynecol Surv*. 1989;44(1):37.

24. Skull AJ, Slater GH, Duncombe JE, Fielding GA. Laparoscopic adjustable banding in pregnancy: Safety, patient tolerance and effect on obesity-related pregnancy outcomes. *Obes Surg*. 2004;14(2):230-235.

25. Ducarme G, Revaux A, Rodrigues A, Aissaoui F, Pharisien I, Uzan M. Obstetric outcome following laparoscopic adjustable gastric banding. *International Journal of Gynecology and Obstetrics*. 2007;98(3):244.

26. Marceau P, Kaufman D, Biron S, et al. Outcome of pregnancies after biliopancreatic diversion. *Obesity Surg*. 2004;14(3):318-324.

27. Wittgrove AC, Jester L, Wittgrove P, Clark GW. Pregnancy following gastric bypass for morbid obesity. *Obesity Surg*. 1998;8(4):461-464.

28. Patel JA, Patel NA, Thomas RL, Nelms JK, Colella JJ. Pregnancy outcomes after laparoscopic roux-en-Y gastric bypass. *Surg Obes Relat Dis*. 2008;4(1):39.

29. Hoff GL, Cai J, Okah FA, Dew PC. Pre-pregnancy overweight status between successive pregnancies and pregnancy outcomes. *J Womens Health (Larchmt)*. 2009;18(9):1413-1417.

30. Mostello D, Jen Chang J, Allen J, Luehr L, Shyken J, Leet T. Recurrent preeclampsia: The effect of weight change between pregnancies. *Obstet Gynecol*. 2010;116(3):667-672.

31. Kling J. Cesarean increase driven by subjective indications. *Obstetrics and Gynecology*. 2011;1:29.

32. McCourt C, Weaver J, Statham H, Beake S, Gamble J, Creedy DK. Elective cesarean section and decision making: A critical review of the literature. *Birth*. 2007;34(1):65-79.

33. Sheiner E, Levy A, Silverberg D, et al. Pregnancy after bariatric surgery is not associated with adverse perinatal outcome. *Obstet Gynecol*. 2004;190(5):1335-40.

34. van Hoorn J, Dekker G, Jeffries B. Gestational diabetes versus obesity as risk factors for pregnancy-induced hypertensive disorders and fetal macrosomia. *Aust NZ J Obs Gynecol* 2002; 42; 35-40.

35. Schaefer-Graf UM, Heuer R, Kilavuz O et al. Maternal obesity not maternal glucose values correlates best with high rates of fetal macrosomia in pregnancies complicated by gestational diabetes. *J Perinat Med* 2002; 30: 313-321.

36. Owen LA, O'Sullivan EP, Kirwan B et al. Atlantic Dip: the impact of obesity on pregnancy outcome in glucose tolerant women. *Diabetes Care* 2010; 33: 577-579.

37. Ehrenberg HM, Durnwald CP, Catalano P et al. The influence of obesity and diabetes on the risk of cesarean delivery. *Am J Obstet Gynecol* 2004; 191: 969-974.

38. Ehrenberg HM, Durnwald CP, Catalano P et al. The influence of obesity and diabetes on the prevalence of macrosomia. *Am J Obstet Gynecol* 2004; 191: 964-968.

39. Wu, G., Bazer, F. W., Cudd, T. A., Meininger, C. J. & Spencer, T. E. Maternal nutrition and fetal development. *J. Nutr.* 2004; 134:2169-2172.

A Systematic Review of the effects of pre-pregnancy weight loss on perinatal outcomes among overweight and obese mothers

Appendix A

Study 1

Study	JAMA Citation: Dixon, JB; Dixon, ME; O'Brian, PE; "Birth Outcomes in Women After Laparoscopic Adjustable Gastric Banding." Obstet Gynecol 2005; 106: 965-72 Country: Australia				
Study Question:	Examine the outcomes of 79 consecutive first pregnancies (>20 weeks of gestation) in women following laparoscopic adjustable gastric banding (LAGB) for severe obesity				
Date of extraction:	6/4/2011				
Source of Funding:	Inamed Health Corporation (the manufacturer of the Lap-Band)				
Source Population	1,382 women who had LAGBs placed between 1/1/1995-8/31/2003				
Study Population	All women (79) in the LAGB program who became pregnant after LABG placement. Exclusion criteria: Only the first pregnancy to each woman post-LAGB was included in the statistical analysis.				
Design	Study Design: Case-control Setting: Sample size: 79				
Potential for selection bias	**Moderate to high** -Study population was as similar to source population as possible as all women from study population who became pregnant had their first pregnancy post-LAGB included in the study, but how close is this? We don't know because the study doesn't give data comparing the study population to the source population. -Are women becoming pregnant after LAGB different from women who did not become pregnant (i.e. younger? lost more weight?) The study did not show how the women who became pregnant post-LAGB differed from women who did not become pregnant. -Is it possible that some women became pregnant without the knowledge of the LAGB group? 2% of the 1,382 women who had LAGBs placed were lost to follow-up, meaning that the study may not have accounted for some pregnancies from the post-LAGB group.				
Population characteristics	Randomization? No Groups similar at baseline? Relatively similar; matched obese cohort was matched for parity, maternal age, and BMI.				
Outcome assessment	Primary outcome measures: Preterm birth? yes IUGR? no Low birth weight? yes Macrosomia? Yes Cesarean section? no Preeclampsia? yes Perinatal morality? no				
Measurement	Study Groups: **N = 79 women with first, post-LAGB singleton pregnancies** **N= 79 severely obese, matched controls** N = 40 penultimate, pre-LAGB pregnancies from the same cohort N = 61,000 state-published birth outcomes ("Births in Victoria, 2001-2002") were used as community controls Exposure measures: Prior record for LAGB procedure already held by institution. Outcomes :Mean birth wt., maternal wt. gain, gestational diabetes, pregnancy-induced HTN, preeclampsia, birth wt, low birth wt., high birth wt., preterm birth, infant M/F ratio Outcome measures: Unspecified. Most likely by medical record review.				
Potential for measurement bias	**Low to Moderate** -LAGB was adjusted during pregnancy in attempt to match maternal weight gains recommended by the Institute of Medicine (confounder?) -The study does not say where the data for birth outcomes was obtained. It could be theorized that they obtained records from each of the hospitals where the patients gave birth, but do these hospitals have standardized procedures for reporting birth outcomes (unequal measures)? Were some reports (e.g. preeclampsia) self-reported?				
Potential for confounding	**Moderate to high** -Women in the LAGB group were not seen a standard number of times. Most women had their bands adjusted at least once during the course of their pregnancies (86%), the rest were not seen for band adjustment during their pregnancies. Outcomes were not stratified to account for these differences. Therefore, the differential control of gestational weight gain could have affected outcomes results among women. -Additionally, for all women who were seen in the LAGB clinic during their 36th wk of gestation, fluid was removed from the gastric band. The study did not provide data for how many women were seen for this visit and how their outcomes differed. - More importantly, the control groups had no such way to control for gestational weight gain, possibly further confounding results. -Women from matched controls may have received significantly different prenatal and obstetric care. No data or information was given about the obese cohort except that they were women presenting for surgery with "obstetric histories". - While some nutritional data was known for the study group (compliance of multivitamin supplementation; anemia; folate, B12, and plasma protein levels), no data was provided for the comparison groups.				
Analysis	-Data were described using mean ± STD for normally distributed variables and median ± interquartile range for other variables and percentages for some ordinal groups. -No discussion or adjustment for confounding, but study did only consider the first pregnancy to each woman following LAGB procedure to minimize oversampling problem of several pregnancies for a single subject.				
Results		Post LAGB	Matched obese	Penultimate/Pre-LAGB	Victorian
	Maternal wt. gain	9.6 ± 9.0 kg	15.5 ± 9.0 kg	14.4 ± 9.7 kg	not reported
	Birth wt.	3,397 ± 545	3,350 ± 1,000	3,350 ± 1,000	3,356
	Low birth wt.	5(6.3%)	7 (8.9%)	not reported	6.9%
	High birth wt.	9 (11.4%)	14 (17.7%)	not reported	11.7%
	Preterm birth	5 (6.3%)	10 (12.7%)	not reported	7.8%
	Preg-induced HTN	8 (10%)	30 (38%)	18 (45%)	10-13%
	Gestational DM	5 (6.3%)	15 (19%)	6 (15%)	5.5%
	Preeclampsia	4 (5%)	20 (25%)	11 (28%)	not reported
Adverse Effects	1 woman developed symptomatic gallstones and had an episode of acute pancreatitis. One woman had persistent vomiting despite removal of the fluid from the band. Two women complained of tenderness over the reservoir site during late pregnancy.				
Attrition	Number of dropouts? None from the study population				
Overall judgment of internal validity (Quality Rating)	Fair				
External validity	Fair; Results likely apply only to morbidly obese women electing to have bariatric surgery for wt. loss, as such drastic weight loss is much more difficult to achieve via other methods.				

Study 2

Study	JAMA Citation: Weintraub, AY.; Levy, A; Levi, I; Mazor, M; Wiznitzer, A; Sheriner, E. "Effect of bariatric surgery on pregnancy outcome." International Journal of Gynecology and Obstetrics, 2008, 103, 3, 246 Country: Israel				
Study Question:	To compare the perinatal outcomes of women who delivered before with women who delivered after bariatric surgery.				
Date of extraction:	6/14/2011				
Source of Funding:	Undisclosed				
Source Population	Over 180,000 singleton deliveries occurring between 1988 and 2006 in the Soroka University Medical Center.				
Study Population:	301 deliveries preceding bariatric surgery and 507 deliveries following bariatric surgery. Exclusion criteria: none specified				
Design	Study Design: Retrospective cohort Setting: Tertiary medical center Sample size: 507 deliveries after bariatric surgery				
Intervention	"…all forms of bariatric surgery, including mainly restrictive but also malabsorptive procedures performed by open or laparoscopic techniques."				
Potential for selection bias	**Low** - No data showing how the two study groups compare to the source population. - Because retrospective data is used, no concern for dropouts, crossovers, etc.				
Population characteristics	Randomization? No Groups similar at baseline? No, pregnancies following bariatric surgery were characterized by advanced maternal age and greater parity and gravidity when compared to pregnancies before bariatric surgery.				
Outcome assessment	Primary outcome measures: Preterm birth? No IUGR? Yes Low birth weight? Yes Macrosomia? Yes Cesarean section? Yes Preeclampsia? Yes Perinatal morality? Yes				
Measurement	Study Groups: N = 301 deliveries before bariatric surgery N = 507 deliveries after bariatric surgery Exposure measures: Not specified where procedures were performed. Outcomes: Birth weight, cesarean delivery, fetal malformations, macrosomia, low birth weight, apgar <7 at 1 min, apgar <7 at 5 min, perinatal mortality, severe preeclampsia, IUGR, gestational DM Outcome measures: Records from the center's perinatal database. Data were reported by an obstetrician directly after delivery.				
Potential for measurement bias	**Low** - Data were reported by an obstetrician directly after delivery at the same medical center. Skilled medical secretaries routinely reviewed the information prior to entering it into the database. Coding was done after assessing the medical prenatal care records together with the routine hospital documents.				
Potential for confounding	**Low to moderate** -Multivariate analysis was used to control for possible confounders. -However not all potential confounders controlled for (e.g. nutritional status, prenatal care)				
Analysis	ORs and 95% confidence intervals were computed.				
Results		Before bariatric surgery	After bariatric surgery	OR	P-value
	Birth weight	3264 ± 599	3079 ± 567	n/a	<0.001
	Cesarean delivery	17.9%	30.0%	1.9	<0.001
	Fetal malformations	3.3%	7.9%	2.5	0.006
	Macrosomia	7.6%	3.2%	0.4	0.004
	Low birth weight	9.0%	11.8%	1.4	0.12
	Perinatal mortality	2.3%	1.0%	0.4	0.11
	Severe preeclampsia	4.0%	1.0%	0.2	0.005
	IUGR	2.3%	3.9%	1.7	0.15
	Gestational DM	11.6%	8.7%	0.7	0.11
Adverse Effects	Higher rate of fetal malformation was not significant after controlling for possible confounders.				
Attrition	Number of dropouts? None				
Overall judgment of internal validity (Quality Rating)	Good				
External validity	Fair; Results likely apply only to morbidly obese women electing to have bariatric surgery for wt. loss, as such drastic weight loss is much more difficult to achieve via other methods. Population in Israel is also rather homogenous, and perhaps not representative of the diversity of the US.				

Study 3

Study	JAMA Citation: Deitel, M.; Stone, E.; Kassam, H.A.; Wilk, E.J.; Sutherland, D.J.A. "Gynecologic-Obstetric Changes after Loss of Massive Excess Weight following Bariatric Surgery" J. Am. Coll. Nutr. 7: 147, 1988. Country: Toronto, Ontario, Canada		
Study Question:	To compare the gynecological/obstetrical disorders after loss of massive excess weight.		
Date of extraction:	6/7/2011		
Source of Funding:	Not reported		
Source Population	138 morbidly obese females who had lost more than 50% of their excess weight following bariatric surgery		
Study Population:	9 patients who tried to conceive after bariatric surgery and subsequent weight loss and who were successful. Exclusion criteria: Not explicitly stated		
Design	Study Design: Prospective cohort Setting: Women who gave birth after bariatric surgery (9 pregnancies) were compared to the 274 pregnancies from the same cohort before bariatric surgery was performed. Sample size: 15 pregnancies		
Intervention	Bariatric surgery (6 by jejunoileal bypass, 23 by horizontal gastroplasty, 109 by vertical banded gastroplasty)		
Potential for selection bias	**High** - No data given to show how similar the women who became pregnant were to the source population. - Study does not state whether they had data for all women in cohort who became pregnant. - No mention of dropouts.		
Population characteristics	Randomization? No Groups similar at baseline? Unknown, no data given comparing groups.		
Outcome assessment	Primary outcome measures: Preterm birth? Yes IUGR? No Low birth weight? No Macrosomia? No Cesarean section? Yes Preeclampsia? Yes Perinatal morality? Yes (spontaneous abortion)		
Measurement	Study Groups: N = 15 pregnancies post-bariatric surgery N = 274 pregnancies Exposure measures: Not specified. Outcomes: irregular menses, hirsutism, urinary stress incontinence, preeclampsia, gestational diabetes, gestational hypertension, venous thrombosis, spontaneous abortions, cesarean section, weight of newborn Outcome measures: Obstetrical history was compiled preoperatively on a standardized form and completed post-operatively (2-5) years after weight loss had been stabilized. Study does not state whether form was self-reported or recorded with assistance.		
Potential for measurement bias	**High** - Measurements likely equal due to standard definitions for each obstetrical outcome, but study does not elaborate. -Significant concern with reliability of measures since the obstetrical history may have been performed with a self-reported form. - Since measurements taken over 2-5 year interval post-surgery, some patients may have had better recall if measurement taken sooner after bariatric surgery. - For some outcomes, data was only given for women who had term pregnancies.		
Potential for confounding	**High** - Prenatal care and nutritional status for women after surgery was not accounted for. If this was significantly different for the post-bariatric surgery group compared to the pregnancies of women before they had bariatric surgery, confounding could occur. - No attempt at matching the groups was made, so differences in age, comorbid disease, race, and other factors may be significant.		
Analysis	Data were described as percentages for ordinal variables and mean ± interquartile range for other variables. No adjustments performed.		
Results		**After weight loss**	**Before bariatric surgery**
	Wt. of newborn	3598.4 ± 354.0 gm	3801.3 ± 771.6 gm
	Spontaneous abortion	6/15 (40%)	69/274 (25.2%)
	Cesarean section	0/9 (0%)	23/205 term pregnancies (11.2%)
	Gestational DM	0/7 (0%)	6/86 (7.0%)
	Gestational HTN	0/7 (0%)	23/86 (26.7%)
	Preeclampsia	0/7 (0%)	11/86 (12.8%)
	Venous thrombosis	0/7 (0%)	6/86 (7.0%)
Adverse Effects	6 spontaneous abortions amongst the weight loss group reported.		
Attrition	Number of dropouts? Not stated		
Overall judgment of internal validity (Quality Rating)	Poor		
External validity	Poor. Results likely apply only to morbidly obese women electing to have bariatric surgery for wt. loss, as such drastic weight loss is much more difficult to achieve via other methods. Furthermore, the study was conducted in 1988 and bariatric surgery and its safety and efficacy have likely changed significantly.		

A Systematic Review of the effects of pre-pregnancy weight loss on perinatal outcomes among overweight and obese mothers

Study 4

Study	JAMA Citation: Skull, A.J.; Slater, G.H.; Duncombe, J.E.; Fielding, G.A. "Laparoscopic Adjustable Banding in Pregnancy: Safety, Patient Tolerance and Effect on Obesity-Related Pregnancy Outcomes" Obesity Surgery, 14, 230-235 Country: Australia			
Study Question:	To determine the safety and outcomes of pregnancies after a laparoscopic adjustable banding (LAGB) procedure by comparing pregnancies before LAGB to pregnancies after LAGB in the same group of women.			
Date of extraction:	6/20/2011			
Source of Funding:	Not disclosed			
Source Population	All women who were included in a computerized database in a particular "unit" (authors do not define what the unit is) and who had been managed through pregnancy between 1996 and 2003.			
Study Population:	44 women with a total of 80 pregnancies Exclusion criteria: Early miscarriages were excluded from analysis.			
Design	Study Design: Case-control study Setting: Sample size: 44 women with a total of 80 pregnancies			
Intervention	LAGB			
Potential for selection bias	**High** -Authors did not include women who were not managed through pregnancy. - Exclusion of early miscarriages could have affected some of the outcomes of the study. - There were differences between the case and control groups in number of 1st pregnancies and mean maternal age due to the design of the study. - Were non-singleton births excluded from analysis?			
Population characteristics	Randomization? No Groups similar at baseline? Yes, but significant differences found for number of 1st pregnancies and mean maternal age between groups.			
Outcome assessment	Primary outcome measures: Preterm birth? No IUGR? No Low birth weight? No Macrosomia? No Cesarean section? Yes Preeclampsia? Yes Perinatal morality? No			
Measurement	Study Groups: N = 31 previous non-LAGB pregnancies N = 49 LAGB pregnancies (historical control group) Exposure measures: Weight related outcomes were collected from the computer database. Outcomes: Pregnancy-induced HTN, Pre-eclampsia, eclampsia, emergency cesarean section, elective cesarean section Outcome measures: Self-reported via questionnaire.			
Potential for measurement bias	**High** - No attempt at standardizing the amount of fluid removed from bands during pregnancy. This would have affected amount of weight gain. - Many outcomes were self-reported through questionnaires, which can be subject to recall bias. - Measurements could be unequal as we do not know if all pregnancies were at same hospital, country, etc.			
Potential for confounding	**Moderate** -Authors do not explicitly state which potential confounders were adjusted for in their analysis, but do state that they used multiple regression was used for "outcomes where a confounding variable could be responsible for the outcome rather than LAGB." - Was age or parity corrected for in analysis? - Nutritional status of patients could have been significantly different. No mention of this in study.			
Analysis	Mean and 95% CIs of the mean were used to determine statistical significance for continuous data, and the Chi-squared test was used for nominal data. Multiple regression was used for outcomes where a confounding variable could be responsible for the outcome rather than LAGB (the paper did not state for which variables this was used).			
Results		LAGB (n = 49)	Non-LAGB (n = 31)	p-value
	Pregnancy-induced HTN	4 (8.1%)	7 (22.5%)	p = 0.06
	Pre-eclampsia	0 (0%)	2 (6.4%)	p = 0.06
	Eclampsia	1 (2%)	1 (3.2%)	p = 0.06
	Emergency cesarean section	2 (4%)	1 (3.2%)	p = 0.1
	Elective cesarean section	12 (24.5%)	3 (9.5%)	p = 0.1
Adverse Effects	2 women in LAGB group had acute gastric prolapse through the band and had the LAGB removed.			
Attrition	Number of dropouts? No			
Overall judgment of internal validity (Quality Rating)	Poor			
External validity	Fair			

Study 5

Study	JAMA Citation: Ducarme, G.; Revaux, A.; Rodrigues, A.; Aissaoui, F.; Pharisien, I.; Uzan, M. " Obstetric outcome following laparoscopic adjustable gastric banding." International Journal of Gynecology and Obstetrics (2007) 28, 244-247. Country: France			
Study Question:	To evaluate obstetric outcomes following laparoscopic adjustable banding (LAGB) in obese women.			
Date of extraction:	6/15/2011			
Source of Funding:	Not stated			
Source Population	All women who delivered at Centre Hospitalier Universitaire Jean Verdier, Bondy, France, from Jan 2004-Oct 2006			
Study Population:	427 obese women (13 who underwent LAGB and 414 who did not) of European descent who had singleton pregnancies. Exclusion criteria: Intrauterine death and fetal loss before 22 weeks; women with a BMI less than 18 were excluded from analysis			
Design	Study Design: Retrospective case-control study Setting: Sample size: 13			
Intervention	LAGB			
Potential for selection bias	**Moderate** - LAGB group and control group relatively similar. -Was there another hospital in the area in which bariatric surgery was more popular (and thus more representative of the population)? - Sampling was limited by the very small number of cases (n = 13). Women who obtained bariatric surgery before pregnancy had a higher BMI before surgery than obese women who did not choose bariatric surgery. Only after surgery were the BMIs not significantly different pre-pregnancy. - Are groups representative of all obese women in the area? Uninsurance may play a role. - No data given with respect to loss to follow-up. Was there loss to follow-up and if so, was it differential?			
Population characteristics	Randomization? No Groups similar at baseline? Fairly similar based on age at conception, weight at conception, BMI, and nulliparity. There was a difference in weight gain during pregnancy due to LAGB procedure.			
Outcome assessment	Primary outcome measures: Preterm birth? Yes IUGR? No Low birth weight? Yes Macrosomia? Yes Cesarean section? Yes Preeclampsia? Yes Perinatal morality? No			
Measurement	Study Groups: N = 13 women (LAGB group) N = 414 women (control group) Exposure measures: Not discussed. Outcomes: Maternal weight gain, preterm delivery, pre-eclampsia, gestational HTN, gestational DM, duration of labor, mode of delivery, induction of labor, low birth weight, small for gestational age, macrosomia, Apgar score at 5 min. Outcome measures: Records from a single hospital were retrospectively reviewed. No information was given as to how this review was performed.			
Potential for measurement bias	**Low to moderate** - All data was obtained from records at the same hospital, so theoretically was reported and recorded similarly. - Was there a standardized procedure in place for reviewing records, and a way to confirm the data? No information was given about the review process.			
Potential for confounding	**Moderate to high** - Paper does not address what the procedure for adjusting the gastric bands in the study group were, or whether this was even done. - Paper does not address nutritional status of both groups, although this information may not have been available from retrospective data. - No mention of an attempt to match controls to study group, although groups were similar with respect to a few listed variables.			
Analysis	- Birth weight listed in g, all other outcomes given as percentages with p-values. - No adjustment for potential confounders was performed.			
Results		LAGB group (n = 13)	Control group (n = 414)	P value
	Birth weight	3271	3305	Not significant
	Preterm birth	7.7	7.1	Not significant
	Low birth weight	7.7	10.6	< 0.05
	Macrosomia	7.7	14.6	< 0.05
	Apgar <7 at 5 min	15.4	13.4	Not significant
	Gestational DM	0	22.1	< 0.05
	Gestational HTN	7.7	8.2	Not significant
	Preeclampsia	0	3.1	< 0.05
	Cesarean delivery	15.3	34.4	< 0.01
Adverse Effects	None stated.			
Attrition	Number of dropouts? Unknown			
Overall judgment of internal validity (Quality Rating)	Fair			
External validity	Fair			

Study 6

Study	JAMA Citation: Marceau, P.; Kaufman, D.; Biron, S.; Hould, F.; Lebel, S.; Marceau, S.; Kral, J.G. "Outcome of Pregnancies after Biliopancreatic Diversion." Obesity Surgery, 14. 318-324. Country: Canada			
Study Question:	The study aims to investigate obstetric outcomes before and after biliopancreatic diversion (BPD) in women who have undergone the procedure due to obesity.			
Date of extraction:	6/15/2011			
Source of Funding:	Not stated			
Source Population	All women who had successfully undergone BPD surgery at Laval Hospital in Quebec (n = 916) more than 2 years earlier than January 2002. This consisted of operations performed between 1984-2000.			
Study Population:	783 women who completed the survey Exclusion criteria: None stated			
Design	Study Design: Retrospective case-control study Setting: Sample size: 132 women gave birth post-BPD resulting in 251 postoperative pregnancies			
Intervention	Biliopancreatic diversion			
Potential for selection bias	**Moderate to high** -783 women, or 85.5% of the 916 women to whom the survey was sent, completed the survey. Was there some difference between the women who completed the surgery and those who did not? - No attempt was made to match the control group to the case group. This could have strengthened the study.			
Population characteristics	Randomization? No Groups similar at baseline? Same group, but age and weight were different based on study design.			
Outcome assessment	Primary outcome measures: Preterm birth? Yes IUGR? No Low birth weight? Yes Macrosomia? Yes Cesarean section? No Preeclampsia? No Perinatal morality? Yes			
Measurement	Study Groups: N = 251 postoperative pregnancies (from 132 women) N = 1,577 preoperative pregnancies (from 594 women) Exposure measures: Records from the hospital in which the BPD surgery was completed. Outcomes: Miscarriages, premature pregnancies, stillbirths, small-for-age, macrosomia Outcome measures: Self-reported via mailed questionnaire			
Potential for measurement bias	**High** -Recall bias is a potential source of bias as the study was done by questionnaire sent by mail. Women had to recall information about birth outcomes. - Differences in numbers of multiple births not accounted for since the study was not limited to only singleton pregnancies. Multiple births in a single pregnancy could affect outcomes such as birth weight. - There was differential reporting of premature pregnancies (1/3 of pre-BPD pregnancies were of unknown duration)			
Potential for confounding	**High** -Differential recall bias based on increased time since preoperative birth. Women may have been able to recall the details of their postoperative births better since less time had elapsed. - Was there a difference in the prenatal care and nutrition between pre- and post-BPD groups. Authors state that they stressed the importance of vitamin supplementation and healthy diet to post-op patients. - Authors do not state any attempt to control for potential confounders.			
Analysis	Values given as means ± SD and p <0.05 considered significant.			
Results		Before BPD surgery (n =1577)	After BPD surgery (n = 251)	Result significant?
	Miscarriages	341 (21.6%)	57 (26%)	Not calculated
	Premature births	141 (16.7%)	22 (13.6%)	Not calculated
	Stillbirths	12 (1.0%)	1 (0.6%)	Not significant
	Small-for-age	20 (3.1%)	15 (9.6%)	Not calculated
	Macrosomia	222 (34.8%)	12 (7.7%)	Not calculated
Adverse Effects	None reported			
Attrition	Number of dropouts?			
Overall judgment of internal validity (Quality Rating)	Poor			
External validity	Fair			

Study 7

Study	JAMA Citation: Wittgrove, A.C.; Jester, L.; Wittgrove, P.; Clark, G.W. "Pregnancy Following Gastric Bypass for Morbid Obesity" Obesity Surgery (1998), 8, 461-464. Country: US		
Study Question:	To review pregnancy-related risks and complications after gastric bypass surgery.		
Date of extraction:	6/21/2011		
Source of Funding:	Not stated		
Source Population	Over 2000 active patients on the bariatric surgery group's (private practice) current newsletter mailing list.		
Study Population:	40 patients who were found to be pregnant and agreed to participate in the study (40/41 agreed). Exclusion criteria: Those not on group's mailing list. Agreeing to participate in study. Statistical analysis was performed on singleton births only.		
Design	Study Design: retrospective case-control Setting: Sample size: 49 pregnancies among 36 women		
Intervention	Primarily Roux-en-Y, some biliopancreatic diversion (BPD)		
Potential for selection bias	**High** - Patients had to contact group. No way to tell how many women who became pregnant did not contact the group. - Excluded women who had elective or spontaneous abortions, which could have affected outcomes. - No attempt at matching groups for any characteristics, and no table 1 showing how similar they are.		
Population characteristics	Randomization? No Groups similar at baseline? Unknown; no data was given as to how the controls matched with the cases, and there was no apparent attempt at matching the groups.		
Outcome assessment	Primary outcome measures: Preterm birth? Yes IUGR? No Low birth weight? No Macrosomia? Yes Cesarean section? Yes Preeclampsia? No Perinatal morality? No		
Measurement	Study Groups: N = 36 postoperative women (cases) N = 17 preoperative women (controls) Exposure measures: Records from surgery group database. Outcomes: preterm labor, hypertension, DM, primary cesarean section, macrosomia Outcome measures: All patients were interviewed by one nurse practitioner, and a standardized form was used for information gathering. Medical records releases were obtained from the patients, so that additional medical information could be reviewed as indicated.		
Potential for measurement bias	**Low to moderate** - All outcomes were recorded in the same manner, listed above. However, self-reported responses can be prone to recall bias. - Some measures, such as preterm labor, were self-reported according to the author.		
Potential for confounding	**High** - Since groups were not matched, there could have been significant differences between the groups such as age, parity, nutritional status, amount of prenatal care, etc. - The study makes no mention of an attempt to adjust for confounding with regards to any variables.		
Analysis	Not stated. The study does not state whether any of the differences found are statistically significant, or whether an attempt was made to determine the statistical significance of the results.		
Results		Preoperative (n = 17)	Postoperative (n = 36)
	Preterm labor	3/23	4/36
	Hypertension	7	0
	Diabetes Mellitus	4	1
	Primary cesarean section	5	5
	Macrosomia	7/23	2/36
Adverse Effects	None stated		
Attrition	Number of dropouts? 0		
Overall judgment of internal validity (Quality Rating)	Poor		
External validity	Fair		

Study 8

Study	JAMA Citation: Patel, J.A.; Patel, N.A.; Thonmas, R.L.; Nelms, J.K.; Colella, J.J. "Pregnancy outcomes after laparoscopic Roux-en-Y gastric bypass" Surgery for Obesity and Related Diseases, 4 (2008), 39-45. Country: US					
Study Question:	To investigate the safety of pregnancies after laparoscopic Roux-en-Y gastric bypass (LRYGB) and its potential effect on obesity-related perinatal complications.					
Date of extraction:	6/21/2011					
Source of Funding:	Authors were compensated by Autosuture					
Source Population	Patients who delivered infants at Allegheny General Hospital between 2003-2006.					
Study Population:	26 patients who delivered after LRYGB Exclusion criteria: None					
Design	Study Design: Retrospective case-control Setting: A community-based, academic, tertiary care center, Sample size: 26					
Intervention	Laparoscopic Roux-en-Y gastric bypass					
Potential for selection bias	**Low** Authors do not state that they attempted to match controls to the cases. However, there were not large differences between the cases and the controls.					
Population characteristics	Randomization? No Groups similar at baseline? LRYGB was significantly older than nonobese and obese controls, had BMI lower than severely obese controls, and a fetal birth weight lower than the severely obese controls, but otherwise there were no significant differences between the case group and the control groups.					
Outcome assessment	Primary outcome measures: Preterm birth? Yes IUGR? Yes Low birth weight? Yes Macrosomia? Yes Cesarean section? Yes Preeclampsia? Yes Perinatal morality? Yes (stillbirth/spontaneous abortion)					
Measurement	Study Groups: N = 26 LRYGB patients (cases) N = 43 Obese controls N = 23 Severely obese controls N = 188 Nonobese controls Exposure measures: Birthing logs were retrospectively reviewed. Outcomes: Primary cesarean section, macrosomia, preeclampsia, preterm delivery, SGA, stillbirth/spontaneous abortion Outcome measures: Charts were reviewed for demographics, delivery route, and pregnancy-related complications.					
Potential for measurement bias	**Low** -Authors do not specify method for performing chart reviews. Was it a standardized process carried out by the same individuals?					
Potential for confounding	**Low to moderate** -No mention of adjusting for any confounders in analysis, such as age. - Women in LRYGB group had regular comprehensive metabolic panels to assess nutritional status, as well as specific instructions about which nutrient rich diet regimens to follow. It is unlikely that the control group was given the same thorough prenatal care concerning constant nutritional status.					
Analysis	Used student t test or chi-square for analysis. P values determined for each comparison.					
Results		LRYGB (cases)	Obese (controls)	Obese p-values	Severely obese (controls)	Severely obese p-values
	Primary C-section	5/8 (62.5%)	0/20 (0%)	n/a	0/23 (0%)	n/a
	Macrosomia	0 (0%)	3 (7.7%)	0.147	5 (18.5%)	0.021
	Preeclampsia	1 (3.8%)	3 (7.7%)	0.527	2 (7.4%)	0.578
	Preterm birth	7 (26.9%)	7 (17.9%)	0.390	7 (25.9%)	0.920
	SGA	3 (11.5%)	1 (2.6%)	0.140	1 (3.7%)	0.279
	Stillbirth/ spontaneous abortion	0 (0%)	0 (0%)	1	2 (7.4%)	0.157
Adverse Effects	2 LRYGB patients required abdominal exploration for small bowel obstruction during their pregnancy.					
Attrition	Number of dropouts? 0					
Overall judgment of internal validity (Quality Rating)	Good					
External validity	Good					

A Systematic Review of the effects of pre-pregnancy weight loss on perinatal outcomes among overweight and obese mothers

Study 9

Study	JAMA Citation: Hoff, G.L.; Cai, J.; Okah, F.A.; Dew, P.C. "Pre-Pregnancy Overweight Status between Successive Pregnancies and Pregnancy Outcomes" J. Women;s Health, 2009, 18, 9, 1413-17. Country: US			
Study Question:	1. To examine factors associated with changes in pre-pregnancy overweight to pre-pregnancy normal/underweight or obese BMI in subsequent pregnancy, and 2. assess select pregnancy and newborn outcomes associated with changes in pre-pregnancy BMI.			
Date of extraction:	6/20/2011			
Source of Funding:	Not stated, but disclosure statement : "No competing financial interests exist."			
Source Population	Female residents of Kansas City, Missouri, who gave birth between 1995-2004.			
Study Population:	1,035 nulliparous women whose pre-pregnancy BMI (25.0-29.9) classified them as overweight. Exclusion criteria: Women who were not nulliparous before 1995. Multiple birth (non-singleton) were also excluded from analysis. Women with a pre-birth BMI <25 or >29.9 before first birth were also excluded.			
Design	Study Design: Retrospective cohort Setting: Sample size: 1,035 women			
Intervention	None			
Potential for selection bias	**Low** -Study population selected from a database of all women giving birth in Kansas City, MO, so it would be representative of all women in that city fitting the study's inclusion criteria. - Table 1 shows the shift from overweight status to normal/underweight status was only statistically significant for difference in low-normal weight gain after multivariable regression correcting for many factors, so groups were statistically similar. - Because retrospective data is used, no concern for dropouts, crossovers, etc.			
Population characteristics	Randomization? No Groups similar at baseline? Yes, except for amount of pregnancy weight gain.			
Outcome assessment	Primary outcome measures: Preterm birth? Yes IUGR? No Low birth weight? No Macrosomia? No Cesarean section? Yes Preeclampsia? No Perinatal morality? No			
Measurement	Study Groups: N = 125 women were normal weight/underweight (BMI <25) before second pregnancy N = 568 women maintained overweight status (BMI 25.0-29.9) before second pregnancy Exposure measures: Information taken from birth certificates regarding women's weight and height so may have been self-reported. Outcomes: Pregnancy HTN, Premature birth, emergency cesarean section, small-for-gestational age (SGA), large-for-gestational age (LGA) Outcome measures: Outcomes data taken from electronic database through the Missouri Department of Health and Senior Services.			
Potential for measurement bias	**Low to moderate** -Authors state that height and weight measurements used for BMI calculations may have been self-reported or self-measured and that women may have underreported weight or over-reported height. - Use of electronic database for birth outcomes are a standardized source of information. - No information given about the data review process.			
Potential for confounding	**Moderate** -Underweight women (BMI <18.5) were included with normal weight women (BMI 18.5-24.9) in analysis. This could change outcome data. However the number of underweight women was not given so we cannot conclude how great the effect on the change on outcomes would be. - Pregnancy weight gain was found to be different between overweight and normal/underweight groups even after multivariable regression analysis.			
Analysis	Multivariable logistic regressions were performed with either obese or normal/underweight as the outcome variable and the aforementioned variables as the independent variables. Multivariable logistic regression also was used to assess risk factors for those pregnancy and newborn outcomes that had a significant second pregnancy distrbution.			
Results		Maintained overweight N = 568	Overweight to Normal/ Underweight N = 125	p value
	Premature birth	32 (5.6%)	11 (8.8%)	>0.05
	Emergency cesarean section	14 (2.5%)	3 (2.4%)	<0.02
	Pregnancy HTN	4 (0.7%)	0 (0%)	>0.05
	SGA	40 (7.0%)	11 (8.8%)	>0.05
	LGA	50 (8.8%)	8 (6.4%)	>0.05
Adverse Effects	None			
Attrition	Number of dropouts? none			
Overall judgment of internal validity (Quality Rating)	Good			
External validity	Good			

Study 10

Study	JAMA Citation: Mostello, D.; Chang, J.J.; Allen, J.; Luehr, L.; Shyken, J.; Leet, T. "Recurrent Preeclampsia: The Effect of Weight Change Between Pregnancies" Obstetrics and Gynecology, 2010, 116, 3, 667-672. Country: US			
Study Question:	To estimate whether the risk of recurrent preeclampsia is affected by interpregnancy change in body mass index.			
Date of extraction:	6/21/2011			
Source of Funding:	"The authors did not report any potential conflicts of interest."			
Source Population	All women who were resident mothers of Missouri who delivered their first two singleton pregnancies at more than 20 weeks of gestation between January 1, 1989, and December 31, 2005.			
Study Population:	17,773 women whose first pregnancies were complicated by preeclampsia Exclusion criteria: Only singleton births were included. Only women who had information required to calculate the prepregnancy BMI for both pregnancies.			
Design	Study Design: Population-based, retrospective cohort Setting: Sample size: 17,773 women			
Intervention	Weight loss by any method			
Potential for selection bias	**Low to moderate** - The study used birth certificates from the Missouri birth certificate registry with a defined definition for preeclampsia. - Only singleton births were included to eliminate the confounding effects of multiple gestation on pregnancy duration, birth weight, and likelihood of preeclampsia. - Some significant differences were observed between groups such as likelihood of obesity, smoking, DM, and premature birth.			
Population characteristics	Randomization? No Groups similar at baseline? There were some significant differences between groups (i.e., age, smoking during pregnancy, and pregnancy interval).			
Outcome assessment	Primary outcome measures: Preterm birth? No IUGR? No Low birth weight? No Macrosomia? No Cesarean section? No Preeclampsia? Yes Perinatal morality? No Maternal weight gain? No			
Measurement	Study Groups: N = 1,471 women decreased BMI between pregnancies N = 8,783 maintained BMI between pregnancies N = 8,798 increased BMI between pregnancies Exposure measures: Data from "maternally linked birth and death certificates" Outcomes: Preeclampsia Outcome measures: Taken from birth certificates			
Potential for measurement bias	**Moderate** - Self-reported values for maternal pre-pregnancy weight and height values were used to calculate pre-pregnancy BMI. - Authors do not detail the method of reviewing birth certificates, nor do they elucidate whether a group of trained individuals reviewed them.			
Potential for confounding	**Low** - Potential confounders, including maternal demographic, medical, and obstetric factors, were included in the multivariable analysis.			
Analysis	Adjusted risk ratios and 95% confidence intervals were calculated using Poisson regression analysis.			
Results		Overall rate of recurrent preeclampsia	Risk ratio	95% Confidence interval
	Women who decreased BMI	12.8%	0.70	0.60 – 0.81
	Women who maintained BMI	14.8%	1	n/a
	Women who increased BMI	18.5%	1.29	1.20-1.38
Adverse Effects	None reported			
Attrition	Number of dropouts? None			
Overall judgment of internal validity (Quality Rating)	Good			
External validity	Good			