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Risks associated with obesity in pregnancy, for the mother and baby: a systematic review of reviews

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No conflict of interest is declared.

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Abbreviations

AOR - adjusted odds ratio

BMI - Body Mass Index

CS - Caesarean section

GDM – Gestational diabetes mellitus

GPCC - Centre for Person-Centred Care, University of Gothenburg

NTD - Neural tube defect

OR – odds ratio

PICOS framework used: Population, intervention, comparison, outcomes and study designs

RCT – Randomised controlled trial

RR – Risk ratio

SSI – Surgical site infection

UK – United Kingdom

US - United States

Abstract

Maternal obesity is linked with adverse outcomes for mothers and babies. To get an overview of risks related to obesity in pregnant women, a systematic review of reviews was conducted. For inclusion, reviews had to compare pregnant women of healthy weight with women with obesity, and measure a health outcome for mother and/or baby. Authors conducted full-text screening, quality assurance using the AMSTAR tool, and data extraction steps in pairs. Narrative analysis of the 22 reviews included show gestational diabetes, pre-eclampsia, gestational hypertension, depression, instrumental and caesarean birth, and surgical site infection to be more likely to occur in pregnant women with obesity compared to women with a healthy weight. Maternal obesity is also linked to greater risk of pre-term birth, large-for-gestational-age babies, fetal defects, congenital anomalies, and perinatal death. Furthermore breastfeeding initiation rates are lower and there is greater risk of early breastfeeding cessation in women with obesity compared with healthy weight women. These adverse outcomes may result in longer duration of hospital stay, with concomitant resource implications. It is crucial to reduce the burden of adverse maternal and fetal/child outcomes caused by maternal obesity. Women with obesity need support to lose weight before they conceive, and to minimise their weight gain in pregnancy.

Introduction

Maternal obesity is becoming an increasing public health issue, and it is known that nutrition and metabolism play a crucial role in the health and wellbeing of both mother and fetus (1). Maternal obesity is reaching epidemic proportions, particularly in the United States (US), where prevalence of obesity in women aged 20-39 years increased from 28.4% in 1999 to 34% in 2008 (2, 3) but has now fallen slightly to 31.9% (4). Across Europe, similar increases from lower starting levels are seen. The latest European Perinatal Health Report showed that the lowest levels of overweight or obesity in pregnant women were in Poland (25.6%), France (27.2%), and Slovenia (27.8%). The majority of other European countries had rates of 30-37%, and Scotland had a prevalence of 48.4%, with 20.7% of all pregnant women in the range of obesity (5).

Maternal obesity is linked with increased rates of caesarean section, depression and medical complications (6). Babies of women with obesity also suffer from pre-term birth, still-birth and fetal anomalies (7). Maternal obesity is the most significant factor leading to obesity in offspring (8) and, coupled with excess weight gain in pregnancy, also results in long-term obesity for women (9).

Several systematic reviews have been conducted in an attempt to synthesise an overall conclusion as to which outcomes can, with certainty, be linked with obesity in pregnancy. These reviews are of differing scope and quality and may, also, have opposing results, leading to confusion among clinicians as to what are the true risks related to maternal obesity. In addition, clinicians (and researchers) may read only one of a number of reviews and base clinical decisions or suggestions for changed practice on this, or ignore the evidence if the review is small, or does not cover their country. The benefit of bringing together a number of systematic reviews on a particular outcome is that the reader is more likely to be convinced by the weight of evidence. Conducting an overview that includes all reviews relating to a topic also ensures that the full range of adverse outcomes for that health issue can be seen in one paper.

Accordingly, our research group set out to conduct a systematic review of systematic reviews, as promoted by the Cochrane Collaboration (10) and described by other papers (11, 12). The aim was to summarise the findings of published systematic reviews regarding the possible risks for pregnant women with obesity, and their infants, compared to pregnant women with a healthy weight and their infants.

Methods

Search strategy

The accepted definitions of obesity (greater than or equal to Body Mass Index (BMI) 30 kg/m²), severe obesity (BMI ≥ 35 kg/m²), and healthy weight between 18.5 and 24.9 kg/m² (13) were planned for use. A protocol was developed *a priori*, outlining the review aim and procedure. An inclusion/exclusion criteria list (based on the PICOS framework in Box 1) was created to identify all the pertinent systematic reviews. This step was done by two reviewers, with additions from the rest of team, and then tested. A comprehensive and systematic search was done in the following databases: PubMed, CINAHL, Cochrane and Scopus, from inception until May 2014, to identify systematic reviews only. The PICOS framework used (population, intervention, comparison, outcomes, study designs) and resulting search string are shown in Box 1.

Box 1: Search string used (for MeSH terms and key words in abstract and title)

PICOS framework and search string
Population: All pregnant women
Intervention: Obesity – as defined by the authors, BMI usually measured before pregnancy or at booking
Comparison: Healthy weight, as defined by the authors
Outcome: Infant or maternal health outcome
Study design: Systematic review or meta-analysis of cohort studies; systematic reviews of intervention/experimental studies if the control groups provided outcomes due to obesity

Search string: (Pregnancy OR "Postpartum Period" OR pregnant OR "post partum" OR postpartum OR "post natal" OR postnatal OR puerperium OR antenatal OR prenatal OR gestation OR gestational OR gravida OR perinatal) AND (Obese OR obesity) AND ("Systematic review" OR "meta-analysis")

Our search was restricted to peer-reviewed articles and we included mainly systematic reviews of cohort studies or case studies, where outcomes were compared for women with obesity and women of healthy weight. We included systematic reviews of intervention/experimental studies if the control groups would provide outcomes due to obesity. All pregnant women were included, with no age, ethnicity or parity restriction, and no language restrictions were used. The outcomes measured had to be health outcomes (risks and complications) for the pregnancy, mother and/or baby. It was not possible to assess publication bias statistically, by funnel plot tests, as review analyses were mixed (e.g., narrative and meta-analyses). Similarly, a meta-analysis was not possible due to heterogeneity between reviews (particularly in relation to differing definitions of obesity and severe obesity), and over-lapping of studies between most reviews, which would have led to double-counting of data.

A total of 638 reviews was found (159 in PubMed, 50 in CINAHL, 37 in Cochrane and 392 in Scopus). Duplicates were excluded and 531 citations were exported to EndNote. A first exclusion by title and abstract was made, based on relevancy, using the inclusion/exclusion criteria, by CB and JM. A second exclusion based on reading the full text was conducted by the whole team, working independently and then comparing opinions in pairs: AD and JM; CB and MB; EO and JM; CB and JM. The reference lists of the 112 remaining full-text reviews were searched for additional citations, with one further review noted. The 113 reviews were divided into four groups, with authors working independently to conduct the full-text screening process (based on our inclusion/exclusion criteria), quality assurance and data extraction steps, and then comparing decisions with their partner. Eighty-six reviews were excluded on full-text screening, as they did not present outcomes for pregnant women with obesity, or they did not compare their findings to pregnant women with a healthy weight (Figure 1).

Quality assessment

The validated AMSTAR tool (14) was used to assess quality of the studies, based on factors such as an *a priori* design, duplicate study selection and data extraction. Each item was given a score of 1 if the specific criterion was met, or 0 if not met, unclear, or not applicable. An overall score relating to review quality was calculated by summing individual item scores. AMSTAR characterises quality at three levels: 8-11 is high quality, 4-7 is medium, 0-3 is low quality (15).

Data extraction

Key findings from each review, potential mechanisms for results, and authors' recommendations were extracted, using a data collection form, by teams of two reviewers. Disagreements were resolved by discussion, or by recourse to a third reviewer. Some reviews included overweight but no data on overweight are presented, due to the overlapping of 'obesity' and 'normal weight' categories described below. Outcomes based on only one study are not presented, as that is not a review. The same search strategy, but not limited to reviews/meta-analyses, was conducted to locate new studies in each topic area to discuss and compare with our findings.

Results:

We excluded 5 studies that received an AMSTAR score of 3 or less (16, 17, 18, 19, 20). This left 22 reviews for analysis, 11 with a quality score of 8 to 11 (21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31), and 11 with a score of 4 to 7 (32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42) (Table 1).

Description of included reviews

Characteristics of the 22 included reviews, with the definitions of obesity used and time in pregnancy that BMI was assessed, are presented in Table 1.

Definitions of obesity used in the reviews differed, possibly due to the change in the Institute of Medicine definition of the obese category from >29 to ≥ 30 in 2009. In addition, one review did not state the definition of obesity (39), 7 reviews had included at least one study with an obesity definition down to BMI 25 kg/m², and 7 included at least one study using a definition of $<29/30$ kg/m², for their “normal BMI” category (Table 1). Authors’ definitions are used throughout.

Reviews were conducted from 2007 to 2014, with included study publication dates ranging from 1969 to 2014. Most reviews involved studies from the United States (US) and United Kingdom (UK), with wide representation of papers from other countries across the world (Table 1). Four reviews presented only a narrative synthesis of results (28, 33, 39, 40) and all others performed meta-analyses of crude or adjusted data.

The number of studies used in all reviews was 624, an average of 28 studies in each systematic review (range 3-70), most of which were case-control or cohort studies. Of these, 51 were overlapping (included in more than one review), giving a total of 573 studies used. The objectives and scope of included reviews varied. Only one concerned general outcomes of maternal obesity; most studied specific fetal outcomes such as still-birth/death/miscarriage (n=4), and congenital disorders (n=3), maternal pregnancy disorders (n=5), and mode of birth (n=3).

Negative health outcomes of obesity in pregnant women

Gestational diabetes mellitus

The association between maternal obesity and gestational diabetes mellitus (GDM) was reported in two reviews (35, 27) published in 2007 and 2009, involving both low- and high-income countries (Table 1). A total of 76 case-control or cohort studies were used after exclusion of over-lapping ones, published from 1992-2006/7. In one of the reviews (35), the estimated risk of developing gestational diabetes was four times higher among women with obesity (unadjusted ratio: 3.05-4.21) and nine times higher (unadjusted ratio: 5.07-16.04) among women with severe obesity (BMI from >33 to >40 kg/m²), compared with normal-weight pregnant women. In the second review (27), similarly, unadjusted ORs were 3.76, 3.01 and 5.55 higher, respectively,

for women with obesity (BMI >29.9 kg/m²), moderate obesity (BMI 30-35 kg/m²), and morbid obesity (BMI >35 kg/m²), when compared with women of normal weight (95% CIs 3.31–4.28, 2.34–3.87, and 4.27–7.21) (27).

Since the review by Torloni et al, published in 2009 (27), other cohort studies in Spain (43), Canada (44), Turkey (45), US (46) and Scotland (47) involving from 931 to 109,592 pregnant women have shown similar findings, that women with obesity are more at risk of GDM. Suggested activities to prevent GDM are diet (48) and physical activity (49), and recent systematic reviews (50, 51) and randomised trials (52, 53) show positive effects of both in reducing GDM.

Pre-eclampsia and hypertension

Two reviews were included. The 54 case-control and cohort studies involved (after exclusion of over-lapping studies) had been conducted in 20 countries, from all continents, between the years of 1995 and 2012 (Table 1). One review found a clear relationship between increasing BMI and risk of pre-eclampsia with pooled RRs for women with obesity (BMI 30-34.9 kg/m², +/- 0.5 unit), and severe obesity (\geq 35 kg/m², +/- 0.5 unit), of 2.68 (95% CI 2.40–3.00) and 3.43 (95% CI 2.59–4.55), respectively (29). The second review used narrative synthesis, and found that women with obesity were 3-10 times more likely to have pre-eclampsia compared with normal weight women, and 4.5-8.7 times more likely to develop gestational hypertension (40). The authors believe many factors could cause this increased risk, such as insulin resistance, genetics, immunology, nutrition, and infective agents, as well as an unhealthy diet and lack of physical activity (40).

Since those reviews, a retrospective study of 120 million women admitted for birth in US hospitals showed an increase in pre-eclampsia rates over 30 years, with obesity listed as one cause for the increase (54). Two cohort studies in Canada (44) and Scotland (47) also observed a positive association between high BMI and gestational hypertension and pre-eclampsia, giving credence to our review's results.

Mode of birth

Three reviews were included in this category (24, 37, 38), based on studies published 1985 to 2007. Many high-income countries were involved, and all reviews included United States (US) and United Kingdom (UK) studies. Sixty-two cohort, case-control and randomised controlled trial (RCT) studies were used, after exclusion of over-lapping studies (Table 1). The unadjusted odds ratio (OR) for women with obesity having CS compared with women of normal weight was found to be from OR 2.01, 95% CI 1.87 – 2.15) (36), up to OR 2.36, 95% CI 2.15-2.59 (23), compared with normal weight pregnant women (Table 2). Similarly, Chu et al (37) found unadjusted ORs in women with obesity (BMI >29 to 39.9) and severe obesity (BMI >35 to >40 kg/m²) of 2.05, 95% CI 1.86–2.27 and 2.89, 95% CI 2.28–3.79, respectively. The Heslehurst review (38) also found increased odds in women with obesity compared with women of ideal weight in instrumental vaginal births (OR 1.17, 95% CI 1.13-1.21) (Table 2).

The increase in CS and instrumental vaginal birth were suggested to be due to: a possible link between increased cholesterol deposits in the myometrium of women with obesity, affecting contractions (24); an increase in maternal soft tissue inside the pelvis narrowing the birth canal and increasing difficult births especially with a macrosomic infant, or a poorer response to oxytocin administration (37).

Associations between obesity and increased rate of CS have been observed in several more recent studies, published after the latest review in 2009 (24). The studies span many different countries and all indicate the same increased rate of CS in women with obesity (43, 45, 47, 55, 56, 57, 58), reinforcing these results.

Surgical site infection

Two reviews were included (33, 39), with a total of 22 studies after over-lapping ones were removed, from 22 countries, published 1990-2012. Both reviews used narrative synthesis. One (39) found a significant association between obesity and surgical site infection (SSI) in two studies only, and four other studies did not find this association. The second review (33) showed that 12 of the 13 studies supported a relationship between obesity and SSI (Table 2).

The two studies demonstrating an association in the first review (39), were not included in the second review (33). Since the latest of those reviews (33), further studies have demonstrated similar results (59, 60) and indicated that these infections may require prophylactic treatment (61).

Mental health

One review and meta-analysis included 62 cohort, case-control, cross-sectional, and intervention studies with 540,373 antenatal or postnatal women from countries worldwide, ranging from 2000-2013 (32) (Table 1). Women with obesity had elevated odds of both antenatal (OR 1.43, 95% CI 1.27–1.61) and postnatal (OR 1.30, 95% CI 1.20–1.42) depression, compared to women of healthy weight. For antenatal anxiety, meta-analysis findings suggested that women with obesity had higher risk compared to healthy weight women (OR 1.41, 95% CI 1.10–1.80). Too few studies were found to merit a meta-analysis for postpartum anxiety, antenatal binge eating disorder and serious mental illness. Qualitative research suggests that women are aware of the elevated health risks associated with their obesity, which may lead to increased anxiety levels (62). Other suggestions for mental ill-health during pregnancy are that pregnant women feel stigmatised for their overweight during pregnancy, which in turn may exacerbate their depression and/or anxiety (23). However, a reverse causal pathway cannot be ruled out, as women with poor mental health also struggle with weight management (23).

Pre-term birth

Three reviews (26, 38, 31) examined links between maternal BMI and pre-term birth, including 133 cohort and case-control studies after over-lapping ones removed. Studies came from more than 45 countries, and were published 1988-2008 (Table 1). One review found a significant increase in the risk of spontaneous pre-term birth <32 weeks gestation for women with BMI ≥ 40 kg/m² (adjusted odds ratio (AOR) 2.27, 95% CI 1.76-2.94). The authors found that, even after adjusting for confounding variables, women with BMI ≥ 35 kg/m² had a 33% higher risk of pre-term birth for all reasons than women with normal weight (AOR 1.33, 95% CI 1.12-1.57)

(26). The second review found that birth at <37 weeks was linked with obesity (OR 1.226, 95% CI 1.149-1.308) and morbid obesity (BMI >40 kg/m²), OR 1.495, 95% CI 1.41-1.59) (38). The third review presented most overweight and obesity results combined; however, the adjusted relative risk of obese and very obese women (BMI ≥34.9 to ≥40 kg/m²) having a pre-term birth before 33 weeks' gestation was 1.49, 95% CI 0.89-2.50, and 2.02, 95% CI 1.24-3.29, respectively, based on pooling 2 studies (31).

More recent studies from Turkey, Sweden and US (45, 63, 64) are generally in line with these results. Reasons are complex and may be influenced by gestational age, race/ethnicity and parity (64), or the interaction of genetic and environmental factors (26). One small study of 253 women in US (65) found opposing results, showing pre-term birth to be decreased in women with obesity, a result that may be due to chance, caused by the small sample size, or due to their definition of pre-term birth as 'before 35 weeks'. Overall, the results of our review appear to show an increase in spontaneous pre-term birth, which may contribute to the increased requirement for neonatal intensive care noted in the Heslehurst review (38).

Infant birth weight

Three reviews of cohort, case-control, and cross-sectional studies were found concerning pre-pregnancy BMI and infant birth weight (30, 38, 31), including 82 studies after over-lapping ones removed. At least 48 countries were involved, but not all reviews provided this information, and publication dates went from 1988-2012 (Table 1). In one review (30), pre-pregnancy obesity decreased the risk of low birth weight (below the 10th centile) (OR 0.81, 95% CI 0.80–0.83) and increased the risk of large for gestational age (above the 90th centile) (OR 2.08, 95% CI 1.95–2.23), compared with normal weight women. Pre-pregnancy obesity also increased the risk of high birth weight (>4,000g) (OR 2.00, 95% CI 1.84–2.18), and macrosomia (>4,500g) (OR 3.23, 95% CI 2.39–4.37). High birth weight (undefined) was also linked with obesity in the second review, (OR 2.357, 95% CI 2.293-2.422) and the risk of low birth weight was decreased (OR 0.84, 95% CI 0.782-0.905) (38).

The third review presented most overweight and obesity results combined (31). The pooled crude data gave a relative risk of having a low birth weight baby (<2,500g) for obese and very obese women (BMI ≥ 34.9 to ≥ 40 kg/m²) as 0.63, 95% CI 0.34 to 1.19, and 0.81, 95% CI 0.42 to 1.53, respectively, based on pooling 4 and 5 studies. Although the review did document the risk of having an extremely low birth weight baby (<1000g) for obese and very obese women separately (31), it was based on one study and so is not presented here. When authors accounted for publication bias, the apparent protective effect of obesity on low birth weight was no longer seen (31).

Since publication of those reviews, a study in Romania (n=500) found a higher incidence of intrauterine growth restriction in pregnancies of women with obesity (66). This unusual finding may be due to chance; a result of the small sample size, or perhaps due to co-morbidity of the mothers. Two large US studies, published since the two reviews (30, 31), found that pregnant women with obesity had reduced odds of having small for gestational age babies (67) or a greater prevalence for large-for-gestational age babies (68). On balance, it would appear that the reviews' (30, 31, 38) conclusion that pre-pregnancy obesity decreases the risk of low birth weight (as all babies of women with obesity tend to be bigger than average) is most likely to be correct, but the effect may be small.

Fetal defects (malformation) and congenital anomalies

Three reviews were included (25, 28, 42), involving at least 11 countries (one study mentioned Scandinavia but did not fully describe the countries). Fourteen cross-sectional, case-control and cohort studies were used excluding ones over-lapping, or non-related to maternal obesity, all published 1969-2010 (Table 1). No effect of BMI was found on esophageal atresia, diaphragmatic hernia, hypospadias, microcephaly, tetralogy of Fallot, transposition of the great arteries or microtia/anotia (25). The prevalence of gastroschisis was significantly lower among mothers who had obesity (OR 0.17, 95% CI 0.10-0.30) (25). Van Lieshout's review included only two relevant studies, neither of which showed any increased risk of fetal alcohol syndrome in babies of mothers with obesity (28). The third review had three studies of relevance

and found a significant association for anorectal anomalies in the fetus of mothers with obesity (OR 1.64, 95% CI 1.35-2.00), based on two studies (42) (Table 2).

It should be noted that two of the reviews (28, 42) were based on only three studies each but the third (25) was larger (18 studies) and of high quality. The review by Van Lieshout et al (28) described limitations of the two studies reviewed, including that the case and control mothers differed in demographic variables such as socio-economic status and education, and the authors had not controlled for important confounders. Confirming the results of the reviews, however, are some recent studies showing an increase in fetal neural tube defects in women with obesity (69, 70, 71, 72). Cardiac defects were also increased in babies of women with obesity in four studies from US, Australia, and Sweden (73, 74, 70, 72). In sum, it would appear that obesity increases the risk of some fetal defects and congenital anomalies. Stothard et al suggested nutritional deficiencies, especially reduced levels of folic acid, as a reason for congenital anomalies. Other possible reasons given were hyperglycaemia and undiagnosed diabetes in pregnant women with obesity. The authors also suggested that, as performing ultrasound scans is more difficult in women with obesity, this could lead to fewer terminations of pregnancy for fetal abnormality (25).

Fetal death, miscarriage and stillbirth

Four reviews investigated the risk of maternal obesity on stillbirth (21, 22, 36), miscarriage (34) and fetal death (21). Observational, cross-sectional, cohort and case-control studies (n=136) were included after overlapping papers were removed, all published 1988-2014. Two of the reviews included studies only from high-income countries (34, 22), the other two included low-income countries in Latin America and Africa also (21, 36) (Table 1). The review of studies on miscarriage showed an association with maternal obesity with a pooled OR for BMI \geq 28 or BMI \geq 30 of 1.31 (1.18-1.46) (34). Fetal death demonstrated a RR for women with a BMI \geq 30 of 1.34 (1.22-1.47), and for those with BMI \geq 35 and \geq 40, RRs of 1.97 (1.71-2.28) and 3.54 (2.56-4.89) (21) (Table 2).

The odds ratio/relative risk of stillbirth in women with obesity (BMI \geq 30 kg/m²) varied from RR 1.46 (1.37-1.55) (20), to AOR 1.6 (1.35-1.95) (21) and OR 2.07 (1.59-2.74) (34). One review found that women with severe (BMI \geq 35 kg/m²) and morbid (BMI \geq 40 kg/m²) obesity had higher RRs for still-birth of 1.78 (1.67-1.91) and 2.19 (2.03-2.36), respectively (21).

The four reviews agreed on many potential mechanisms for the results found. Two agree on the point that obesity during pregnancy itself increases the risk for maternal co-morbidities that are risk factors for stillbirth and miscarriage (21, 36). Another theory discussed in two reviews was the possibility that thinner women could have a better ability to feel a decrease in fetal movements, and would thus seek care as soon as movements declined (21, 36).

We found three studies published after those reviews. Two supported the relationship between maternal obesity and increased rates of neonatal/perinatal death (75, 45), and a large cohort study of singleton births (n=2,868,482) found rates of stillbirth increased with increasing BMI (76), thus confirming our review's results.

Miscellaneous outcomes

One moderate-quality review (38), involving 49 studies from 15 countries, published 1990-2007 (Table 1), found an increased risk of birth over 41 to 42 weeks gestation, increased rates of induction of labour, more frequent use of oxytocin augmentation and higher incidence of failure to progress in labour in women with obesity compared with those of healthy weight (38). Also found was that babies of women with obesity needed neonatal intensive care more often, and had higher rates of fetal compromise and meconium stained liquor. Women with obesity compared with those of ideal weight had a higher risk of postpartum haemorrhage and a longer duration of hospital stay (2.84 days (95% CI 2.77-2.91) compared with 2.4 days for normal weight women) (Table 2).

Longer duration of hospital stay in women with obesity has also been found in Scottish (47), and Australian (9) studies, which leads to higher healthcare costs (77). Denison et al (47) computed extra costs to the Scottish health services to be £59.89

(£41.61-78.17), £202.46 (£178.61-226.31), and £350.75 (£284.82-416.69), respectively, for women who were overweight (BMI 25 <30 kg/m²), obese (30 <40 kg/m²), or severely obese (≥40 kg/m²) (euro and dollar equivalents €75.33/\$94.27, €254.64/\$318.67 and €441.15/\$552.08 respectively).

Breastfeeding

Two systematic reviews, of moderate quality, were included (32, 41), with 29 studies from nine different countries, when the 11 overlapping studies were removed. Cohort studies, surveys, reviews of medical records, and database studies were considered, all published 1989-2011 (Table 1). Women with obesity were less likely to initiate breastfeeding than normal weight women, with ORs from 1.38-3.09 in one review (32) and 1.19-3.65 in the second (41). Seven out of 15 studies in one review (32) found that women with obesity breastfed for a shorter duration than did women with normal weight, and the second found an increase in early cessation of breastfeeding, with a range of hazard ratios from 1.24-2.54 (41) (Table 2).

The review authors suggest the reasons that women with obesity may have difficulty in breastfeeding may be physiological, behavioural, socio-cultural, psychological and medical (32, 41). For example, women with obesity may have elevated progesterone levels which may prevent the usual fall in progesterone following birth that leads to lactogenesis (32). Large breasts may also make latching on more difficult (32). There may also be complex socio-cultural reasons why women with obesity are less likely to breastfeed successfully, such as lower socio-economic group, not having been breastfed themselves, smoking, low self-esteem, poor mental health or solely that they may feel more uncomfortable breastfeeding in public (32).

Studies published after the most recent review (41) confirm that women with obesity had lower initiation rates and were at greater risk of stopping breastfeeding than women of normal weight (78, 79, 80, 81, 82, 83). One study found that women with high pre-pregnant BMI tend to breastfeed for shorter durations due to lack of comfort or confidence with their body image (79).

Discussion

This review of reviews has presented the health risks for women with obesity and their fetuses/babies. Risks include gestational diabetes (identified as a risk factor in one moderate and one high-quality review, based on 76 studies (27, 35)), gestational hypertension and pre-eclampsia (54 studies in one moderate and one high-quality review (40, 29)), and mental ill-health expressed as antenatal anxiety and depression, and postpartum depression (62 studies in one high-quality review (23)). At birth, the odds for caesarean section were increased, ranging from 2-2.36 in three included reviews (37, 38, 24), one of high quality and two of moderate, including 62 studies. An increase in instrumental birth was also noted (38).

Surgical site infection was increased after CS (two reviews (33, 39) using narrative synthesis only and both of moderate quality, based on 22 studies). Breastfeeding was less likely to be initiated and/or maintained (two moderate-quality reviews (32, 41), based on 29 studies, with findings corroborated by recent research (78, 79)).

The health risks for babies of mothers with obesity include an increase in the risk of pre-term birth (<32, <33 and <37 weeks gestation) for all women with obesity, shown in the one moderate and two high-quality reviews identified (26, 31, 38), based on 133 studies. Also found was an increase in the risk of larger 'large for gestational age' babies (30, 38) and a decrease in the risk of low birth weight (30), in the one moderate and one high-quality review, covering 82 studies. Two reviews (25, 42), one moderate and one high-quality, based on 14 studies, found that obesity in mothers pre- and during pregnancy was a significant predictor of neurodevelopmental problems or malformations in the children (Table 2). These problems include 'neural tube defect (NTD), anencephaly, spina bifida, cardiovascular anomaly, septal anomaly, cleft palate, cleft lip and palate, anorectal atresia, hydrocephaly, limb reduction anomaly" (25, p.646) and anorectal anomalies (42), but not fetal alcohol syndrome (28). In addition, four reviews (two moderate and two high-quality, including 136 studies) found that maternal obesity increased the incidence of stillbirth (21, 36, 22), miscarriage (34) and fetal death (21), and more recent studies supported these results (45, 75, 76).

A key cause for women with obesity having higher rates of GDM is that they tend to have a less healthy diet and take less physical activity. As authors of two reviews also believe that hyperglycaemia, undiagnosed diabetes (25) or nutritional deficiencies (25, 42) may be causative factors for fetal malformation, increased promotion of taking folic acid, a healthy diet and sufficient exercise for all women planning pregnancy should be instigated, as a matter of policy. Women should also be supported, through national subsidised programmes, to lose weight before they conceive and to control their weight in pregnancy. Research into this area of care is currently scant (84, 85) and indicates that weight advice is seldom provided (86). Despite this, there are some promising intervention findings regarding women's improvements in healthy eating and physical activity (87, 88). Interventions targeting pregnant women with obesity should take into consideration the potential poor mental health of these women, who may have disordered eating and thus need extra support (89). In relation to breastfeeding, clinicians do not appear to provide extra support (90) to women with obesity, nor do they always seek help (78), so health care professionals need to identify women who may struggle breastfeeding, and provide extra assistance.

Comprehensive, updated systematic reviews on gestational diabetes in women with obesity, the risk of CSs and instrumental births to women with obesity, and the risk of pre-term birth should now be repeated, as the latest studies in reviews considered here were published in 2006-8. A revised systematic review on pre-eclampsia in women with obesity, including the results of three large recent studies (44, 47, 54), would also be useful. Although two narrative reviews presented here showed that surgical site infection was increased in women with obesity (33, 39), five studies in those reviews showed no association, and more recent studies have been conducted (59, 60). There is, therefore, a need for a new systematic review on SSI in relation to obesity in pregnancy, including a meta-analysis, if possible.

Further research is needed into the causes and management of depression in pregnant and postpartum women with obesity, particularly as there may be a reverse causal pathway, where women with poor mental health have difficulty with weight management (23). More research is also needed on specific interventions targeting

the reduction of gestational diabetes in women with obesity, and into how race, ethnicity and parity may influence rates of pre-term birth.

As many of the studies included in the reviews on breast-feeding did not control for confounding variables (32), further research is needed. More qualitative studies are also recommended regarding these women's perspective in order to understand their infant feeding decisions and behaviour (41, 32). Recent trials of interventions such as peer counselling or extra support targeted at women with overweight or obesity (91, 92) did not find it improved breastfeeding rates or continuation of breastfeeding. However, as a Cochrane systematic review has shown that such support given to women irrespective of weight status is effective (93), further research is needed to develop feasible and acceptable interventions for women with obesity.

Review strengths and limitations

To our knowledge, this is the first review of reviews summarising the risks associated with maternal obesity. The key strength is the amount and quality of literature from all languages that has been gathered together, summarised and discussed critically, including reference to recent trial results. The result is a succinct, exhaustive and extensive review that includes both mother and baby outcomes, and physical and mental health. The inability to perform a meta-analysis is a limitation, but was not possible due to heterogeneity between reviews (particularly in relation to differing definitions of obesity and severe obesity), and over-lapping of studies between most reviews, which would have led to double-counting of data. We have limited the outcomes to maternal obesity compared to normal weight pregnant women without reference to women who are overweight, as some studies included in the reviews had 'overweight' categories that overlapped with normal or obese definitions. We have not used grey literature, but think it unlikely that there are unpublished systematic reviews in this area. Importantly, we focused on maternal obesity, but excessive gestational weight gain may also be an issue, that can exacerbate some of these health risks.

Conclusions and recommendations

The negative impact of obesity before and during pregnancy on mothers' and their babies' health is clear. Health conditions such as gestational diabetes, pre-eclampsia and gestational hypertension are common in pregnant women with obesity. There is also an increased rate of instrumental and caesarean section births, and a greater rate of surgical site infections and antenatal and postnatal depression. The risk of large for gestational age babies is higher, and lower breastfeeding initiation rates and shorter breastfeeding duration are also seen. In addition, obesity is linked to a greater risk of pre-term birth, fetal defects, congenital anomalies, and perinatal death. These adverse outcomes lead to increased costs, due to longer duration of hospital stay and higher treatment costs. Investing in national subsidised programmes aimed at supporting women to lose weight before they conceive, and control their weight in pregnancy, may thus confer long-term health and monetary benefits.

Research that is needed in this area, in addition to updates systematic reviews, includes: qualitative studies on women's perspectives of breastfeeding, in order to understand their infant feeding decisions and behaviour, and explorations of why pregnant women with obesity suffer from poorer mental health compared to those of healthy weight. Research into effective pre-conception interventions to help women with obesity lose weight before they conceive, and between pregnancies, is also essential, in order to reduce the burden of maternal and fetal outcomes caused by maternal obesity.

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Figure 1: Study flow diagram

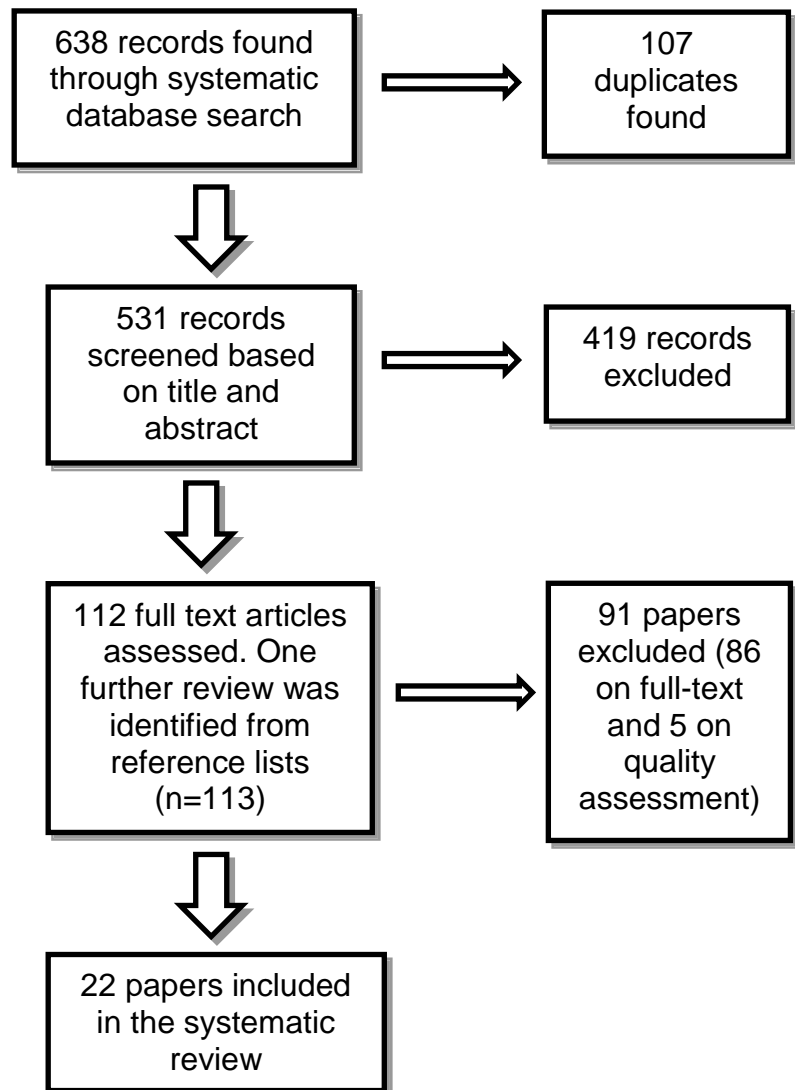


Table 1. Characteristics of 22 included reviews

First author, Year AMSTAR score	Time frame of searches , and date range of included studies	Scope of review	Population (data on overweight excluded)	Range of definitions of 'normal BMI' used by included studies	Range of definitions of 'obesity' used by included studies	Time BMI measured/ assessed in pregnancy	Number of included studies Sample size	Location: countries or group of countries	Type of studies included
Amir, 2007 Score: 4	Inception to Jan/Feb 2007 Range 1989-2006	Breast feeding intention, initiation and duration	Pregnant women with data on maternal obesity and lactation/ breast feeding	20-25 kg/m ² – lowest <26.1 kg/m ² – highest	25- <30 kg/m ² – lowest BMI > 30 kg/m ² - highest	Pre-pregnancy (8); 'at time of interview' (3); post-partum (2); antenatal booking (1); not stated (2)	16 studies (22 in full review) (N = N/A)	US, Australia, Russia, Kuwait, Denmark	Cohort studies, surveys, medical records and database studies
Anderson, 2013 Score: 8	2002 to 2012 Range 2002-2012	Risk of surgical site infection (SSI)	Pregnant women with obesity undergoing caesarean section.	19.8-24.9 kg/m ² – lowest ≤30 kg/m ² – highest	≥25 kg/m ² – lowest > 30 kg/m ² - highest	Admission to hospital (2); pre-pregnancy (2); BMI gain during pregnancy (1) Time not stated (8)	13 studies (N = 225,949)	UK, US, Canada, Israel, Norway, Denmark, Nigeria, Egypt, India, China	Cohort, case-control study, nested case-control study, register study
Aune, 2014 Score: 9	Inception to Jan 2014 Range 1992-2014	Risk of fetal death, stillbirth, perinatal, neonatal and infant death	Women with BMI reported before or in early pregnancy	18.5-<23 kg/m ² – lowest 19.8 - 26 kg/m ² – highest	≥25 kg/m ² – lowest >30 kg/m ² - highest	Pre-pregnancy or early in pregnancy	38 studies (44 publications) (N = N/A)	UK, Sweden, Denmark, Latin America, India, Finland, Korea, England, Spain Australia, US, China,	Cohort studies

								Canada, Argentina, Zambia, Northern Ireland, Scotland	
Boots, 2011 Score: 6	1948 to 2011 Range 1988-2010	Risk of miscarriage	Women with obesity (BMI ≥ 28 / ≥ 30) who conceived spontaneously	18.5 – 24.9 kg/m ² – lowest 19 – 24.9 kg/m ² – highest	≥ 28 kg/m ² – lowest ≥ 30 kg/m ² – highest	Time not stated (6)	6 studies (N= 28,538)	US, Canada, UK	Cohort , Case-control studies
Chu, 2007 (a) Score: 4	1980 to Jan 2006 Range 1992-2006	Risk of GDM	Pregnant women with obesity and severe obesity	18–24.9 kg/m ² – lowest 22–28 kg/m ² – highest	>29 kg/m ² – lowest >35 kg/m ² – highest	Pre-pregnancy or during the first trimester or first prenatal visit	20 studies (N= 844,295)	US, Canada, Australia, Italy, France, United Arab Emirates, Israel, Finland, Nova Scotia, UK	Case Control or Cohort studies (pro- and retro-spective)
Chu, 2007 (b) Score: 4	1980 to Sep 2005 Range 1993-2005	Risk of stillbirth	Women with BMI reported before, or in, pregnancy	18.1–22 kg/m ² – lowest 22–28 kg/m ² – highest	29.1-35 kg/m ² – lowest >30 kg/m ² – highest	Pre-pregnancy or during the first trimester or first prenatal	9 studies (N= 1,031,804)	US, Sweden, Norway, Benin, Denmark, United Arab Emirates, UK, France	Cohort or case-control studies
Chu, 2007 (c) Score: 4	1980 to 2005 Range 1985-2005	Risk of caesarean birth	Maternal obesity	18.5–24.9 kg/m ² – lowest <29 kg/m ² – highest	29–39.9 kg/m ² – lowest >35 kg/m ² – highest	Pre-pregnancy or during the first trimester or first prenatal visit	33 studies (N= 1,391,654)	US, Sweden, France, Denmark, Israel, Canada, UK, Poland, United Arab Emirates	Cohort, Case-control studies
Flenady, 2011 Score: 8	1998 to 2009 Range	Risk factors for stillbirth in high	Population-based studies addressing	<25 kg/m ²	> 30 kg/m	Second trimester, or at	4 studies (96 in the full review)	US, Sweden, UK	Cohort, Case-control

	1993-2009	income countries	risk factors for stillbirth			booking	(N = N/A)		studies
Heslehurst 2008 Score: 7	1990 to 2007 Range 1990-2007	Impact on short-term obstetric and neonatal outcomes in women with obesity	Pregnant women with maternal weight or BMI recorded < 16 gestational weeks	18–24.9 kg/m ² lowest 20–30 kg/m ² – highest	25-30 kg/m ² – lowest >30 kg/m ² - highest	First trimester (recorded before 16 weeks of pregnancy)	49 studies (N = N/A)	Abu Dhabi, Australia, UK, Austria, Brazil, Canada, Iran, Denmark, Italy, Finland, France, Israel , Sweden, Thailand, USA	Cohort studies
Lakhan, 2010 Score: 5	1990 to 2007 Range 1990-2006	Risk of surgical site infection (SSI) following CS	Women who had caesarean section	Not stated	Not stated	Time not stated	9 studies (15 in full review) (N = N/A)	Italy, New Zealand, Saudi Arabia, UK, USA, Vietnam	Prospective observational cohort studies; RCTs
McDonald, 2010 Score: 9	1950 - 2009 Range 1989-2008	Risk of preterm birth and low birth weight.	Women with obesity and preterm birth (<37 weeks) or low birth weight (<2500 g)	18.3–29.8 kg/m ² – lowest <29 kg/m ² – highest	>24 kg/m ² – lowest >40 kg/m ² - highest	Time not stated for the 5 studies included in this review	(5 studies (84 in full review) N= 1,095, 834	Not stated for the 5 studies included in this review	Cohort and case control studies
Molyneaux, 2014 Score: 9	Inception to Jan 2013 Range 2000-2013	Risk of antenatal and postpartum mental disorders	Studies assessing antenatal or postpartum mental disorders in women with obesity	18.5–25 kg/m ² – lowest 20- 25 kg/m ² highest	>29 kg/m ² – lowest >32.3 kg/m ² - highest	1 year before pregnancy or during the first trimester	62 studies (N=75,108)	North America, Australasia, South America, Asia, Europe (not fully reported)	Cohort, Case-control, Cross-sectional, and Intervention studies
Poobalan, 2009 Score: 8	1996 to 2007 Range 1998-	Increasing maternal BMI and risk of elective/	Nulliparous pregnant women with obesity	19.8–26 kg/m ² – lowest 20–30 kg/m ² –	>29 kg/m ² – lowest >30 kg/m ² - highest	Pre-pregnancy or at booking visit	11 studies (N=20,419)	USA, UK, Denmark, Sweden	Cohort studies (3 prospective)

	2007	emergency caesarean birth		highest					
Salihi, 2012 Score: 5	1992 to Dec 2011 Range 1995-2011	Risk of pre-eclampsia, casual mechanism or pathway	Pregnant women	18.5–24.99 kg/m ² – lowest <25 kg/m ² – highest	>30 kg/m ² – lowest >45 kg/m ² - highest	Pre-pregnancy (15); first trimester (2); booking visit (1); postpartum (1); time not stated (2)	21 studies (N = N/A)	Italy, Germany, Australia, Israel, France, Saudi Arabia, Canada, Netherlands, Zimbabwe, US, Denmark, UK, Sweden, Czech Republic, Pakistan, Brazil	Prospective cohort studies
Stothard, 2009 Score: 9	1966 to 2008 Range 1969-2007	Risk of congenital anomaly	Women with pre-pregnancy/early pregnancy weight/BMI measured	18.1–28.3 kg/m ² – lowest ≤29 kg/m ² – highest	≥28 kg/m ² – lowest ≥31kg/m ² - highest	Pre-pregnancy (26); booking visit (6); 2 nd trimester (1); time not stated (7)	39 in full review, 18 in meta-analysis (N = N/A)	UK, US , Canada, Sweden, Spain, Australia	Case control, Cohort studies
Torloni, 2009 (a) Score: 9	1968 to Jan 2008 Range 1988-2008	Risk of preterm birth (PTB)	Unselected or low-risk women with pre-gravid BMI measured	20-24.9 kg/m ² (categories for individual studies not given)	>30kg/m ² (categories for individual studies not given)	Pre-pregnancy BMI	39 studies (40 articles) (N= 1,788,633)	32 from developed countries (not fully reported) and the rest from Argentina, Iran, Mexico, United Arab Emirates, Qatar, Trinidad	Cohort, Case-control studies

Torloni, 2009 (b) Score: 10	1977 to March 2007 Range 1992-2007	Risk of GDM	Women with pre-pregnancy or first trimester BMI measured	<18.5 kg/m ² – lowest <30 kg/m ² – highest	25 –29.9 kg/m ² – lowest >32.9 kg/m ² - highest	Pre-pregnancy or first trimester BMI	70 studies (N= 671,945)	53 high-income and 17 low-middle-income countries (not fully reported).	Case-control, Cohort studies
Turcksin, 2012 Score: 5	1996 (or 1997) to 2011 Range 1997-2011	Breast feeding	Low-risk mothers with obesity or normal weight	18.5–24.9 kg/m ² - lowest 19.8–26.0 kg/m ² - highest	>29.0 kg/m ² - lowest ≥30.0 kg/m ² - highest	Pre-pregnancy (13); at time of interview (postpartum) (4); time not stated (2)	18 studies (19 papers) (N = N/A)	US, Australia, Russia, Denmark, Greece, France, Belgium	Pro- and retrospective cohort studies
Van Lieshout, 2011 Score: 8	From inception to Sep 2010 Range 1998-2010	Risk of neuro-developmental problems in offspring	All pregnant women	19-29 kg/m ² – lowest 20–27 kg/m ² - highest	>29 kg/m ² – lowest >30 kg/m ² - highest	Pre-pregnancy (7); first (2), second (2), or third (1) trimester (self-reported or measured)	3 studies (12 in the full review) (N = N/A)	US, Finland, South Africa, Scandinavia (not fully reported) Sweden, US, Japan, Italy, Australia	Case-control, Cohort studies
Wang, 2013 Score: 10	Inception to Jun 2012 Range 1997-2012	Risk of pre-eclampsia	Pregnant women	20-24.9 kg/m ² (+/- 0.5 unit deviation)	30-34.9 kg/m ² (+/- 0.5 unit deviation)	Pre-pregnancy or early pregnancy	29 studies (N= 1,980,761)	US, Australia, Netherlands, Brazil, Sweden, Denmark, Norway, Israel, Argentina, Saudi Arabia, Ireland, New Zealand, UK	Prospective cohort studies
Yu, 2013 Score: 9	1970 to Nov 2012	Birth weight of infants	All pregnant women	18.5–22.9 kg/m ² – lowest	≥25 kg/m ² – lowest ≥30 kg/m ² -	Pre-pregnancy	45 studies (N = N/A)	UK, Sweden, Denmark, USA,	Cohort, Case-control, and

	Range 2001- 2012			19.8–26 kg/m ² – highest	highest			Germany, Saudi Arabia, China, Turkey, South Australia, Iran, Sudan, Korea, India, Thailand, Italy, Pakistan, France, Canada, Croatia	Cross- sectional studies
Zwink, 2011 Score: 7	N/A Range 1981- 2010	Risk of anorectal mal- formations in offspring	All pregnant women	18.5 - <25 kg/m ²	≥30.0 kg/m ²	Pre- pregnancy	3 studies (22 in full review) (N = N/A)	US, Sweden, Netherlands	Case- control, Cross- sectional studies

RCT=randomised controlled trial, PTB=preterm birth, GDM=gestational diabetes mellitus, N/A=not available

Table 2. Outcomes of maternal obesity compared with normal maternal BMI

First author, Year	Key findings reported OR/RR (95% Confidence Interval)	Potential mechanisms suggested by authors	Recommendations made by authors
Gestational diabetes mellitus (GDM)			
Chu, 2007 (a)	GDM, adjusted ORs: BMI ≥ 30, 3.34 (2.43–4.55) BMI ≥ 35, 5.77 (3.60 –9.39)	Numerous studies have reported an increased risk of gestational diabetes mellitus (GDM) among women who are overweight or obese compared with normal-weight women.	Prevention strategies, aimed at both individual and societal levels. Screen women at an early stage for preexisting diabetes and to counsel women about type 2 diabetes prevention in the postpartum period.
Torloni, 2009 (b)	GDM, unadjusted OR: All BMI ≥ 30, 3.76 BMI 30- 34.9, 3.01 BMI ≥ 35, 5.55 GDM increased 0.92% for every 1 kg m ⁻² increase in women's BMI	Changes in maternal intermediary metabolism. Insulin receptors and post-receptor defects associated with obesity may be further exacerbated by pregnancy. A systemic inflammation seems to be involved as indicated by higher levels of serum C-reactive protein, interleukin-6 and ferritin. As adipocytes secrete pro-inflammatory cytokines, inflammation is usually associated with obesity. Therefore, the abundance of adipocytes in obese women could produce excess inflammatory markers that in turn would lead to the development of GDM.	Obesity is a possibly modifiable risk factor, so obese women should be informed about their risks and supported to lose weight prior to conception.
Pre-eclampsia and hypertension			
Salihi, 2012	Narrative synthesis: BMI ≥ 30 were 3-10 times more likely to have pre-eclampsia BMI ≥ 30 were 4.5-8.7 times more likely to develop gestational hypertension	Insulin resistance, genetics, immunology, nutrition, and infective agents may cause pre-eclampsia, as may failure of the trophoblast cells to invade the myometrium, oxidative stress, endothelial dysfunction, calcitrophic hormone dysfunction, release of growth factors, antiangiogenic proteins.	More research on causative factors and development of effective preventive interventions.
Wang, 2013	Pre-eclampsia, pooled OR: BMI ≥ 30, 2.68 (2.40–3.00) BMI ≥ 35, 3.43 (2.59–4.55)	Autonomic function, hyperactivity of the sympathetic nervous system may influence blood pressure directly, alterations in metabolic functions, including insulin resistance, diabetes, dyslipidemia and increased blood pressure, oxidative stress and chronic inflammation, which can increase the risk of pre-eclampsia.	Further research to determine efficacy of antenatal diet or lifestyle interventions to prevent pre-eclampsia and identify the best choice for women with high BMI.
Mode of birth			

Chu, 2007 (c)	Caesarean birth, unadjusted ORs: BMI ≥ 30, 2.05 (1.86–2.27) BMI ≥ 35, 2.89 (2.28–3.79)	Increased maternal pelvic soft tissue narrows the diameters of the birth canal and increases the risks associated with dystocia, a macrosomic infant, or cephalopelvic disproportion or differences in labour progression or response to oxytocin administration.	Further research to understand the mechanisms between maternal BMI and CS.
Heslehurst, 2008	Total CS, OR: BMI ≥ 30, 2.01 (1.87-2.15); BMI ≥ 35, 1.43 (1.35-1.52) Elective CS: BMI ≥ 30, 1.24 (0.90-1.71) (NS) Emergency CS: BMI ≥ 30, 1.63 (1.40-1.89) Instrumental vaginal birth: BMI ≥ 30, 1.17 (1.13-1.21)	Larger babies may contribute to failure to progress in the first or second stages of labour, and may require instrumental vaginal births or emergency CS.	Developing a successful programme of public health interventions to prevent maternal obesity and clinical guidelines for the care of women with high BMI.
Poobalan, 2009	Total CS, unadjusted pooled OR: BMI ≥ 30, 2.26 (2.04 - 2.51) BMI ≥ 35, 3.38 (2.49-4.57) Elective CS, pooled OR: BMI ≥ 30, 1.87 (1.64-2.12) Emergency CS, unadjusted pooled OR: BMI ≥ 30, 2.23 (2.07-2.42)	Possible link between increased cholesterol deposits in the myometrium of obese women and the increased risk of CS.	Further research on restricted weight gain during pregnancy.
Surgical site infection (SSI)			
Anderson, 2013	Synthesis of integrative review: 12 out of 13 studies supported a relationship between obesity and SSI	Obesity can result in serious post-operative complications for child bearing women undergoing caesarean section such as SSI.	Community midwives could implement wound assessments post-discharge, when SSI is often detected.
Lakhan, 2010	Narrative synthesis Overall SSI, OR: BMI ≥ 30, 2.13 (1.08–4.18) and 2.0 (1.3–3.0) in two studies, four studies showed no association.	The lack of consistency in the risk factors studied may have influenced the risk factors found to be independently associated with SSI.	Future research to test a CS-specific risk index for surveillance purposes, ultimately enhancing quality of care for women undergoing CS.
Mental health			
Molyneaux, 2014	Raised depression symptoms, pooled OR: BMI ≥ 30, 1.43 (1.27–1.61) Elevated depression symptoms, pooled OR: BMI ≥ 30, 1.30 (1.20–1.42) Antenatal anxiety, pooled OR: BMI ≥ 30, 1.41 (1.10–1.80)	Weight stigmatization, physical ill health, low socioeconomic status, and poor diet may contribute to effect on mental disorders. Gestational diabetes or backache in pregnancy may also increase the association. Also, women with a history of depression may gain weight before pregnancy, due to the obesogenic effect of many antipsychotics or antidepressants, or to over-eating.	Further research on risk of gestational diabetes and preeclampsia, on behavioral change interventions for pregnant or postpartum women the effect of obesity on women's health behaviors and change in their behaviour.
Pre-term birth			

Heslehurst, 2008	PTB (<32 weeks), OR: BMI ≥ 30, 1.59 (1.47-1.72)		
McDonald, 2010	PTB (< 37 weeks) Overall risk of PTB in women with obesity or normal weight was similar. PTB (<33 weeks): Adjusted OR BMI 30 to 34.9, 1.49 (0.89-2.50) BMI ≥ 34.9 to ≥ 40, 2.02 (1.24-3.29)	The presence of confounding variables related to obesity and preterm birth might explain some of the results. Studies in this review tried to modify this effect by exclusion, matching, using multiple regression to control for some variables, or by comparing some variables between the two groups (obesity and normal weight).	Monitoring PTB should be considered in overweight and obese women. Further research should be done to investigate the reason why obese women are at risk of PTB and to develop better weight loss programmes for women of childbearing age before
Torloni, 2009 (a)	Spontaneous PTB, adjusted OR: BMI ≥ 30, 0.83 (0.75-0.92) PTB 32-36 weeks, adjusted OR: BMI ≥ 30, 1.60 (1.32-1.94), BMI ≥ 35, 2.43 (1.46-4.05) PTB in general, adjusted OR: BMI ≥ 35, 1.33 (1.12-1.57) PTB < 32 weeks, adjusted OR: BMI ≥ 40, 2.27 (1.76-2.94)	Interaction between genetic and environmental factors. High maternal BMI may have different effects on different types of PTB. A short cervix is significantly lower among obese compared to normal or underweight women and this may in part explain their reduced risk for spontaneous PTB. Increased nutrient intake may also act as a protective mechanism against spontaneous PTB.	Further research to analyze the association between high maternal BMI and subtypes of PTB, spontaneous PTB, with intact or premature rupture of membranes, as well as elective PTB.
Infant birth weight			
Heslehurst, 2008	LBW, OR: BMI ≥ 30, 0.81 (0.78-0.91), BMI ≥ 35, NS HBW, OR: BMI ≥ 30, 2.36 (2.29-2.42)		National guidelines for clinical practice are urgently needed for the management of pregnant women with BMI ≥ 30. Develop public health interventions to prevent maternal obesity.
McDonald, 2010	LBW (<2500 g), RR: BMI 30 to 34.9, 0.63 (0.34 to 1.19) BMI ≥ 34.9 to ≥ 40, 0.81 (0.42 to 1.53)	The presence of confounding variables related to obesity and low birth weight might explain some of the results. Studies in this review tried to modify this effect (see above). When authors accounted for publication bias, by addition of nine imputed studies, the apparent protective effect of obesity on low birth weight was no longer seen.	Health personnel need to be aware that obesity in women is not necessarily protective against having LBW.
Yu, 2013	LBW (<2,500 g), OR: Pre-pregnancy BMI ≥ 30, 0.81 (0.80–0.83) LGA (above the 90th percentile) , OR: Pre-pregnancy BMI ≥ 30, 2.08 (1.95–2.23) HBW (>4,000 g), OR:	Nutrition in the mother can change the structure, physiology, and metabolism in the fetus, predisposing that child for high BMI in adulthood. Malnutrition or over-nutrition during pregnancy may cause epigenetic changes in the fetus/baby, which	Recognition of the association between obesity and birthweight has implications for education of mothers to reduce pre-pregnancy BMI.

	Pre-pregnancy BMI \geq 30, 2.00 (1.84–2.18) Macrosomia (>4,500 g), OR: Pre-pregnancy BMI \geq 30, 3.23 (2.39–4.37) Overweight/obesity in the child, OR: Pre-pregnancy BMI \geq 30, 3.06 (2.68–3.49)	may affect health in adulthood.	
Fetal defects (malformation) and congenital anomalies			
Stothard, 2009	All malformation risks related to BMI \geq 30, OR: Neural tube defect, 1.87 (1.62-2.15); Anencephaly, 1.39 (1.03-1.87); Spina bifida, 2.24 (1.86-2.69); Cardiovascular anomaly, 1.30 (1.12-1.51); Septal anomaly, 1.20 (1.09-1.31); Cleft palate, 1.23 (1.03-1.47); Cleft lip and palate, 1.20 (1.03-1.40); Anorectal atresia, 1.48 (1.12-1.97); Hydrocephaly, 1.68 (1.19-2.36); Limb reduction anomaly, 1.34 (1.03-1.73); Gastroschisis, 0.17 (0.10-0.30)	Undiagnosed diabetes and hyperglycemia in obese pregnant women. Nutritional deficiencies, especially reduced folate levels (for NTD) and other deficiencies for other congenital anomalies. Ultrasound scanning more difficult in obese women, so maybe fewer terminations for FA.	Primary prevention strategies for offspring overweight/obesity by targeting maternal pre-pregnancy BMI. Further research powered to investigate the complete range of BMI to investigate the possible pattern of dose response.
Van Lieshout, 2011	Narrative review Study 1: Unadjusted <i>t</i> -test showed significant difference between BMI in mothers of foetal alcohol syndrome children (24.9) and control mothers (27.5), <i>P</i> = 0.019. Study 2: Unadjusted ANOVA showed significant difference between BMI in mothers of foetal alcohol syndrome children (22.5) and control mothers (27.4), <i>P</i> = 0.001.	Case and control mothers differed in a number of important ways including socio-economic status, education etc. Authors did not control for important confounders.	Strategies designed to reduce pre-pregnancy obesity and to help women reach and maintain healthy weights during pregnancy for the primary prevention of congenital problems.
Zwink, 2011	Significant association for anorectal anomalies in the fetus, OR: BMI \geq 30, 1.64 (1.35-2.00)		Need to develop large-scale multicentre registers of affected infants – basis for more studies
Fetal death/miscarriage/stillbirth			
Aune, 2014	Fetal death, RR: BMI \geq 30, 1.34 (1.22-1.47), BMI \geq 35, 1.97 (1.71-2.28), BMI \geq 40, 3.54 (2.56-4.89) Stillbirth, RR: BMI \geq 30, 1.46 (1.37-1.55), BMI \geq 35, 1.78 (1.67-1.91), BMI \geq 40, 2.19 (2.03-2.36)	An underlying biological relationship between maternal adiposity and fetal and infant death. High BMI is associated with increased risk of preeclampsia, gestational diabetes, type 2 diabetes, gestational hypertension, and congenital anomalies. Decreased possibility to feel fetal movements. Placental dysfunction among obese women.	Weight management guidelines for women who plan pregnancies.
Boots,	Miscarriage, pooled OR:	A possible positive correlation between increasing	More studies are urgently needed

2011	BMI \geq 28 or BMI \geq 30, 1.31 (1.18-1.46)	BMI and the risk of miscarriage.	to verify these preliminary results
Chu, 2007 (b)	Stillbirth, OR: BMI \geq 30, 2.07 (1.59-2.74)	Increased risk of GDM and hypertensive disorders, both risk factors for stillbirth. Maybe decreased possibility to feel fetal movements. More extended periods of snoring, more apnea-hypoxia.	Encourage obese women to undertake a weight reduction program before attempting pregnancy.
Flenady, 2011	Stillbirth, adjusted OR: BMI \geq 30, 1.6 (1.35-1.95)	Placental pathology important contributor to stillbirth in high-income countries. A substantial proportion of stillbirths in such countries lack an obvious maternal risk factor and are thought most likely to reflect an incompletely understood abnormality of placental function, which might or might not be associated with impaired growth.	Weight management before, during, and after pregnancy. Awareness of the risks associated with common pre-gestational and gestational medical disorders.
Miscellaneous outcomes			
Heslehurst, 2008	Neonatal intensive care use, OR: BMI \geq 30, 1.38 (1.16-1.64), BMI \geq 35, 1.33 (1.18-1.51) Fetal compromise, OR: BMI \geq 30, 1.62 (1.54-1.70), BMI \geq 35, 2.08 (1.92-2.25) Meconium, OR: BMI \geq 30, 1.57 (1.42-1.73) Postpartum hemorrhage, OR: BMI \geq 30, 1.20 (1.16-1.24), BMI \geq 35, 1.43 (1.33-1.54) Placenta previa, OR: BMI \geq 30, 0.83 (0.71-0.96) Shoulder dystocia, OR: BMI \geq 30, 1.04 (0.97-1.12), NS Third and fourth degree tears, NS Length of hospital stay (mean days), OR: BMI \geq 30, 2.71 (2.62-2.79), BMI \geq 35, 3.28 (3.13-3.43) Postdate birth (>41/42 weeks), OR: BMI \geq 30, 1.37 (1.33-1.41), BMI \geq 35, 1.56 (1.48-1.64) Induction of labour, OR: BMI \geq 30, 1.88 (1.84-1.92) Oxytocin augmentation, OR: BMI \geq 30, 1.59 (1.36-1.87) Failure to progress, OR: BMI \geq 30, 2.31 (1.87-	Larger babies may contribute to failure to progress in the first or second stages of labour, and may require instrumental vaginal births or emergency CS.	Developing a successful programme of public health interventions to prevent maternal obesity and clinical guidelines for the care of women with high BMI.

	2.82)		
Breast feeding			
Amir, 2007	<p>Women with BMI \geq 30, compared with normal weight women Not commencing breast feeding, range of ORs: 1.38 to 3.09</p> <p>Seven out of 15 studies found that women with obesity breastfed for a shorter duration than did women with normal weight</p>	<p>Obesity is associated with delayed lactogenesis. As this review also showed that women with obesity intend to breastfeed for shorter durations than other women, perhaps part of the delay in time to first feed and tendency to give up before hospital discharge is behavioural rather than physiological.</p>	<p>Qualitative studies from women's perspective as well as quantitative studies are necessary, to explore the relationship between maternal obesity and breastfeeding.</p>
Turcksin, 2012	<p>Women with BMI \geq 30, compared with normal weight women Initiation of breastfeeding, range of ORs (10 studies): 1.19 to 3.65 Low milk transfer at 60 hrs, range of ORs: 6.14 (1.10-37.41) Early cessation of breastfeeding, range of hazard ratios: 1.24 to 2.54</p>	<p>Maternal obesity is associated with a decreased intention and initiation of breastfeeding, a shortened duration of breastfeeding, a less adequate milk supply and a delayed onset of lactogenesis. Larger breasts can be a mechanical barrier to put the baby to the breast, and can therefore have a negative influence on the milk production and secretion.</p>	<p>Additional education for health care professionals. Breastfeeding promotion interventions and counselling practices targeting women with BMI \geq 30, and assistance for breastfeeding, starting before conception until 6 months post-partum.</p>

CS= caesarean section, SSI=surgical site infection, PTB=preterm birth, LBW=low birth weight, HBW=high birth weight, LGA=large for gestational age, OR=odds ratio (95% confidence interval), RR=relative risk, HR=hazard ratio, FA = folic acid, NTD = neural tube defect