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Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Shanshan Han¹, Caroline A Crowther¹, Philippa Middleton¹

¹ARCH: Australian Research Centre for Health of Women and Babies, Discipline of Obstetrics and Gynaecology, The University of Adelaide, Adelaide, Australia

Contact address: Shanshan Han, ARCH: Australian Research Centre for Health of Women and Babies, Discipline of Obstetrics and Gynaecology, The University of Adelaide, Women's and Children's Hospital, 72 King William Road, Adelaide, South Australia, 5006, Australia. shan.han@adelaide.edu.au.

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ABSTRACT

Background

Pregnancy hyperglycaemia without meeting gestational diabetes mellitus (GDM) diagnostic criteria affects a significant proportion of pregnant women each year. It is associated with a range of adverse pregnancy outcomes. Although intensive management for women with GDM has been proven beneficial for women and their babies, there is little known about the effects of treating women with hyperglycaemia who do not meet diagnostic criteria for GDM and type 2 diabetes (T2DM).

Objectives

To assess the effects of different types of management strategies for pregnant women with hyperglycaemia not meeting diagnostic criteria for GDM and T2DM (referred as borderline GDM in this review).

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 September 2011).

Selection criteria

Randomised and cluster-randomised trials comparing alternative management strategies for women with borderline GDM.

Data collection and analysis

Two review authors independently assessed study eligibility, extracted data and assessed risk of bias of included studies. Data were checked for accuracy.
Main results

We included four trials involving 543 women and their babies (but only data from 521 women and their babies is included in our analyses). Three of the four included studies had moderate to high risk of bias and one study was at low to moderate risk of bias. Babies born to women receiving management for borderline GDM (generally dietary counselling and metabolic monitoring) were less likely to be macrosomic (birthweight greater than 4000 g) (three trials, 438 infants, risk ratio (RR) 0.38, 95% confidence interval (CI) 0.19 to 0.74) or large-for-gestational (LGA) age (three trials, 438 infants, RR 0.37, 95% CI 0.20 to 0.66) when compared with those born to women in the routine care group. There were no significant differences in rates of caesarean section (three trials, 509 women, RR 0.93, 95% CI 0.68 to 1.27) and operative vaginal birth (one trial, 83 women, RR 1.37, 95% CI 0.20 to 9.27) between the two groups.

Authors’ conclusions

This review found interventions including providing dietary advice and blood glucose level monitoring for women with pregnancy hyperglycaemia not meeting GDM and T2DM diagnostic criteria helped reduce the number of macrosomic and LGA babies without increasing caesarean section and operative vaginal birth rates. It is important to notice that the results of this review were based on four small randomised trials with moderate to high risk of bias without follow-up outcomes for both women and their babies.

Plain language summary

Management of pregnant women with borderline gestational diabetes mellitus

Gestational diabetes mellitus (GDM) is usually said to be any degree of glucose intolerance or high blood glucose level (hyperglycaemia) that is first recognised during pregnancy. Yet no immediately obvious cut-off points can be labelled as abnormal. It is unclear when treatment should be provided to normalise the blood glucose, as the relationship between increased hyperglycaemia and adverse pregnancy outcomes appears to be continuous. Pre-eclampsia in the mother, birthweight greater than 4000 g (macrosomia), birth trauma with large-for-gestational age (LGA) babies, and a future risk of obesity and diabetes in the mothers and babies are all associated with hyperglycaemia during pregnancy. Intensive management involving lifestyle interventions and metabolic monitoring for women with GDM has been proven beneficial for women and their babies.

This review found dietary advice or counselling and blood glucose level monitoring for women with borderline GDM helped reduce the number of macrosomic and LGA babies. A single trial found that the interventions led to more inductions of labour. The interventions did not increase the risk of caesarean sections, operative vaginal births or women’s weight gain in pregnancy. These findings were based on four small randomised controlled trials (involving 543 women). The trials were of moderate to high risk of bias and only data from 521 women and their babies is included in our analyses. Until additional evidence from large well designed randomised trials becomes available, current evidence is insufficient to make conclusive recommendations for the management of women with pregnancy high blood glucose concentrations not meeting GDM (or type 2 diabetes) diagnostic criteria.

Background

Description of the condition

Introduction and definition of pregnancy hyperglycaemia meeting and without meeting GDM diagnostic criteria

Gestational diabetes mellitus (GDM) is usually defined as ‘any degree of glucose intolerance or any severity of hyperglycaemia (high blood glucose level) with onset or first recognition during pregnancy’ (Metzger 1998; WHO 1999). Therefore, GDM may include previously undetected type 1 (T1DM) or type 2 (T2DM) diabetes or diabetes presenting only during pregnancy (Metzger 1998).

Screening for GDM is usually by either a universal screening procedure (all pregnant women are screened for GDM) or a selective risk-related procedure (only pregnant women with one or
more risk factors for GDM are screened) (ADA 2009). Regardless of which policy is used for screening, the diagnosis of GDM is usually based on either a 75-gram two-hour oral glucose tolerance test (OGTT) or a 100-gram three-hour OGTT (ADA 2009; Hoffman 1998; IADPSG 2010; NICE 2008; WHO 1999). However, different health bodies recommend slightly different criteria for GDM diagnosis in regard to OGTT, which means different populations of women are labelled as having GDM in different parts of the world (IADPSG 2010). Moreover, the recommendations on GDM diagnostic criteria have changed over time, sometimes due to the changing understanding about the effects of hyperglycaemia on pregnancy outcomes (Coustan 2010).

Some women have glucose concentrations that do not meet diagnostic criteria for GDM, but which are toward the upper end of the recommended normal range. As for women with GDM, these women are at increased risk of adverse pregnancy outcomes. Interventions lowering blood glucose concentrations may be beneficial for them.

Aetiology of pregnancy hyperglycaemia

Insulin, secreted by pancreatic beta cells in response to increasing blood glucose concentrations, helps to maintain normal concentrations. Either inadequate insulin secretion (such as in T1DM) or insulin resistance (defined as insulin acting less effectively in promoting glucose uptake) (such as in T2DM or GDM) can result in hyperglycaemia.

Insulin resistance increases with advancing gestation (Clapp 2006). Hormones secreted from the placenta, including tumour necrosis factor-alpha (TNF-α), placental lactogen, placental growth hormone, cortisol and progesterone are thought to be the likely triggers of these physiological changes (Clapp 2006; Devlieger 2008). Increasing insulin resistance in pregnancy, especially during the third trimester, helps to meet the increased nutrient requirement for fetal development and promotes fetal growth by increasing maternal glucose supply (Devlieger 2008). Hyperglycaemia during pregnancy occurs when the insulin secretion is inadequate for the degree of insulin resistance (Clapp 2006).

Epidemiology of pregnancy hyperglycaemia

The prevalence of GDM is rising worldwide with 1% to 14% of pregnancies being affected (Botallico 2007; Dabelea 2005; Ferrara 2007; Ragnarsdottir 2010). In low-risk populations, the estimated GDM prevalence is 1.4% to 2.8% (Mulla 2010); in higher risk populations, the estimated prevalence is 3.3% to 6.1% and in some high-risk populations, the prevalence may be higher than 10% (Mulla 2010).

Few data are available on the prevalence of pregnancy hyperglycaemia which does not meet GDM diagnostic criteria. Data from Australian studies suggest that in addition to the 5.5% to 8.8% women with GDM, a further 7% of all pregnant women have hyperglycaemia not meeting GDM diagnostic criteria each year (normal 75-gram OGTT was defined as fasting blood glucose less than 5.5 mmol/L, and two-hour blood glucose less than 7.8 mmol/L) (Dodd 2007; Ju 2008). Results from a US study indicated the prevalence of pregnancy hyperglycaemia without meeting GDM diagnostic criteria was about 8.8% (normal 100-gram OGTT was defined as fasting glucose less than 5.6 mmol/L (100 mg/dL); one-hour glucose less than 10.6 mmol/L (190 mg/dL); two-hour glucose less than 9.2 (165 mg/dL); three-hour glucose less than 8.1 (145 mg/dL) (Stamilio 2004).

Risk factors for pregnancy hyperglycaemia

There are a range of known risk factors for hyperglycaemic disorders during pregnancy. Advanced maternal age and maternal overweight/obesity are among the most common risk factors (Morisset 2010). Women with some specific ethnicities are at higher risk of developing pregnancy hyperglycaemia; these include African-American, Asian-American, Native American, African, Hispanic, Asian, Pacific Islander, and Indigenous Australian (ADA 2009; Ben-Haroush 2004; Hoffman 1998; Petry 2010). Other risk factors include: history of having a macrosomic (birthweight 4000 g or more) infant, history of GDM, family history of diabetes mellitus, maternal high or low birthweight, high parity, polycystic ovarian syndrome and cigarette smoking (Cypryk 2008; Petry 2010; Solomon 1997). Diet and lifestyle factors, such as low fibre and high glycaemic load diet and physical inactivity, are also associated with an increased risk of pregnancy hyperglycaemia (Chasan-Taber 2008; Zhang 2006).

Clinical outcomes for women with pregnancy hyperglycaemia

Pregnancy hyperglycaemia affects both mothers and their babies. The effects of maternal hyperglycaemia on the pregnancy outcomes do not occur at specific thresholds but are increased on a continuum with increasing hyperglycaemia (Metzger 2008).

1) Maternal outcomes related to pregnancy hyperglycaemia

For women with pregnancy hyperglycaemia, there is an increased risk of developing pre-eclampsia and an increased use of induction of labour (Anderberg 2010; Crowther 2005; Dodd 2007; Ju 2008; Landon 2009; Metzger 2008; Sermer 1998). The risk of having caesarean section is also increased (Dodd 2007; Landon 2009; Metzger 2008; Sermer 1998). Due to the risk of having a large-for-gestational-age (LGA) or macrosomic baby, mothers are at higher risk of cephalopelvic disproportion, uterine rupture, shoulder dystocia and perineal lacerations (Jastrow 2010). Evidence from a systematic review showed hyperglycaemia in pregnancy was highly predictive for the later development of diabetes, with more than 50% of women with GDM developing type 2 diabetes mellitus within 10 years of the index pregnancy (Kim 2002).
There are a range of known health risks associated with pregnancy hyperglycaemia without meeting GDM diagnostic criteria. A large multicentre and multiethnic cohort study (HAPO study) of 25,505 women assessed the effect of maternal hyperglycaemia on pregnancy outcomes (Metzger 2008). This study found a significant, continuous association between maternal glucose concentrations below those for a diagnosis of GDM and caesarean section and pre-eclampsia (Metzger 2008). Similarly, data from 16,975 women who gave birth at a tertiary Australian hospital from 1993 to 2003 showed that women with borderline GDM had increased risk of pre-eclampsia and caesarean section, and their infants were at increased risk of hypoglycaemia and hyperbilirubinaemia compared with women having normal glucose tolerance and their babies (Dodd 2007). Borderline GDM was defined as a positive OGCT (blood glucose 7.8 mmol/L or more; one hour after a 50 g glucose load) and a normal 75 g OGTT (fasting blood glucose less than 5.5 mmol/L and two-hour blood glucose less than 7.8 mmol/L) (Dodd 2007). Another Australian study that recruited 1804 primiparous women from four different states assessed the effect of borderline GDM (blood glucose 7.8 mmol/L or more one hour after a 50 g glucose load) and a normal 75 g OGTT (fasting blood glucose less than 5.5 mmol/L and two-hour blood glucose less than 7.8 mmol/L) on pregnancy outcomes (Ju 2008). Women with borderline GDM were at increased risk of a serious maternal outcome, pregnancy hypertension and caesarean section (Ju 2008).

2) Neonatal, infant and later outcomes related to pregnancy hyperglycaemia

Any degree of maternal hyperglycaemia, whether meeting GDM diagnostic criteria or not, exposes the fetus to an intrauterine environment of increased concentrations of glucose through transplacental passage (Reece 2009). As maternal insulin does not cross the placenta from the mother to fetus, the fetus is forced to increase its own insulin secretion (Reece 2009). Excessive insulin produced by the fetus may lead to fetal over-growth, known as LGA; or a birthweight of 4000 g or more (Ju 2008; Metzger 2008; Reece 2009). Birthweight of 4000 g or more, known as macrosomia, complicates about 50% of pregnancies with GDM, which includes women with optimal glycaemic control through interventions (Catalano 2003). Moreover, babies born to women with pregnancy hyperglycaemia have significantly greater skinfold measures and fat mass compared with infants of women with normal glucose tolerance (Catalano 2003; McFarland 1998; Vohr 1997). Being a LGA fetus or macroscopic infant is a surrogate for many of the complications associated with pregnancy hyperglycaemia (Esakoff 2009; Metzger 2008). Babies who are LGA or macroscopic are at increased risk of injury during birth, such as shoulder dystocia, perinatal asphyxia, bone fractures and nerve palsy (Henriksen 2008; Langer 2005; Metzger 2008). After birth, babies of women with hyperglycaemic disorders are at higher risk of having other neonatal complications such as respiratory distress syndrome, hypoglycaemia, hyperbilirubinaemia (increased levels of bilirubin in the blood), cardiomyopathy (the deterioration of the function of the myocardium), hypocalcaemia, hypomagnesaemia, polycythemia, hyperviscosity and admission to neonatal nursery (Ju 2008; Metzger 2008; Reece 2009; Soler 1978).

In the longer term, children born to mothers with hyperglycaemia are at increased risk of being overweight or obese in childhood and adulthood regardless of their birthweight, developing T1DM and T2DM and having impaired intellectual achievement (Harder 2009; Mulla 2010; Pettit 1985; Rizzo 1997; Whincup 2008; Yogev 2009).

At every age measured, the offspring of women with GDM are heavier (adjusted for height) and higher adiposity than the offspring of women with normal glycaemia during pregnancy (Pettit 1983; Pettit 1985; Vohr 1997; Vohr 1999). In addition, there is a positive trend for increasing childhood obesity at age of five to seven years across the range of increasing maternal hyperglycaemia during pregnancy, which remained after adjustment for maternal weight gain, maternal age, parity, ethnicity and birthweight (Hillier 2007).

Infants born LGA are also at increased risk of developing the metabolic syndrome (a cluster of risk factors defined by the occurrence of three of the following: obesity, hypertension, hypertriglyceridaemia and low high-density lipoprotein cholesterol concentration) in childhood, adolescence and adulthood (Barker 1994; Guerrero-Romero 2010; Harder 2009). Childhood development of the metabolic syndrome predicts adult T2DM at 25 to 30 years of age (Morrison 2008). These health problems continue across generations (Mulla 2010; Pettit 1985). Evidence also shows LGA and macrosomia may be associated with increased risk of developmental delay (Ornoy 2005; Rizzo 1997; Slining 2010) and premenopausal breast cancer (Forman 2005).

Description of the intervention

Treatment for pregnancy hyperglycaemia

The primary aims of treatment for pregnancy hyperglycaemia are to optimise glycaemic control and improve pregnancy outcomes (Aliwan 2009). Management includes any or all of: diet and exercise advice, use of oral glucose-lowering agents (e.g. metformin, glyburide), administration of insulin, fetal surveillance (e.g. doppler umbilical blood flow measurement, cardiotocograph and ultrasonography) and maternal glucose monitoring (Hoffman 1998; Metzger 2007).

Providing dietary and exercise advice is usually recommended as the primary therapeutic strategy for women with GDM to achieve acceptable glycaemic control (ACOG 2001; Hoffman 1998; NICE 2008). Evidence from randomised controlled trials
had suggested that diet and exercise interventions were effective in improving pregnancy outcomes for women with pregnancy hyperglycaemia (Bonomo 2005; Crowther 2005; Landon 2009). If these interventions alone are not enough to achieve good maternal glycaemic control, insulin therapy may be indicated (ACOG 2001; Hoffman 1998; NICE 2008). Oral hypoglycaemics such as glyburide and metformin have been used as alternatives to insulin therapy (Alwan 2009; Silva 2010; Simmons 2004). As a part of management for GDM, maternal glucose monitoring is always used for guiding treatment and ultrasonography helps to guide management of birth (ACOG 2001; Hoffman 1998).

A Cochrane review assessed the effect of these management interventions for women with GDM on maternal and infant outcomes (Alwan 2009), and found such management was effective and beneficial for women with GDM and their infants (Alwan 2009). Similar findings were reported in another systematic review on the effects of treatment in women with GDM (Horvath 2010). What is uncertain is whether these interventions are beneficial for women with a lower degree of pregnancy hyperglycaemia (Landon 2010; Sacks 2009).

**Why it is important to do this review**

Pregnancy hyperglycaemia without meeting GDM diagnostic criteria affects a significant proportion of pregnant women (Dodd 2007; Ju 2008; Rumbold 2006; Stamilio 2004). Hyperglycaemia during pregnancy is associated with adverse pregnancy outcomes including macrosomia, respiratory distress syndrome and future development of obesity and T1DM or T2DM in the offspring (Dabelea 2000; Dabelea 2007; Harder 2009; Hillier 2007; Metzger 2008; Silverman 1995) and pre-eclampsia, birth trauma, and development of type 2 diabetes in the mother (Kim 2002; Metzger 2008). The relationship between increased hyperglycaemia and the adverse pregnancy outcomes appears to be continuous (Metzger 2008; Mulla 2010). There are no immediately obvious cut-off points which can be labelled as abnormal to diagnose GDM (Metzger 2008; Mulla 2010). It is therefore unclear at what degree of pregnancy hyperglycaemia ‘treatment’ should be provided to normalise blood glucose. Although intensive management of GDM has been proven beneficial for women with GDM and their babies (Alwan 2009; Crowther 2005; Horvath 2010; Landon 2009), there is little known about the effects of managing women with hyperglycaemia who do not meet diagnostic criteria for GDM and T2DM. This review aims to provide reliable evidence to guide the best care for women with pregnancy hyperglycaemia not meeting GDM diagnostic criteria.

**Objectives**

To assess the effects of different types of management strategies for pregnant women with hyperglycaemia not meeting diagnostic criteria for gestational diabetes mellitus (GDM) and type 2 diabetes (referred to as borderline GDM in this review).

**Methods**

**Criteria for considering studies for this review**

**Types of studies**

All published randomised controlled trials (RCTs) and cluster-randomised trials comparing alternative management strategies for women with borderline gestational diabetes mellitus (GDM). We intended to include published abstracts for RCTs and cluster-RCTs if relevant outcome data were available. We planned to exclude quasi-RCTs and crossover trials.

**Types of participants**

Pregnant women with hyperglycaemia who do not meet the diagnostic criteria for GDM. Diagnostic criteria for GDM based on oral glucose tolerance test results are defined variously by individual trialists according to local health authorities and professional organisations. Women were eligible regardless of gestation, age, parity or plurality. Women with pre-existing diabetes mellitus and previously treated GDM were not eligible. We intended to included trials that included pregnant women with normal glycaemia, GDM or pre-existing diabetes mellitus if we could extract subgroup data for women with hyperglycaemia not meeting diagnostic criteria separately.

**Types of interventions**

We planned to include any form of management for women with pregnancy hyperglycaemia not meeting GDM diagnostic criteria above routine antenatal care in the review. These included any type of dietary advice (standard or individualised), exercise and lifestyle advice (standard or individualised) and drug treatment including insulin and oral drugs.

One type of intervention compared with standard antenatal care. These included: any type of dietary advice (standard or individualised) compared with standard antenatal care; any type of exercise advice (standard or individualised) compared with standard antenatal care; drug treatment compared with standard antenatal care. Multiple forms of intervention compared with standard care, i.e. diet and exercise advice compared with standard antenatal care;
diet and exercise advice and drug treatment compared with standard antenatal care. Two forms of management would be compared against each other, i.e. diet and exercise advice compared with drug treatment. Two or more types of the same form of management could be compared against each other, i.e. standard dietary advice compared with individualised dietary advice; standard exercise advice compared with individualised exercise advice; different types of dietary advice could be compared with each other; insulin treatment could be compared with oral drug treatment.

Types of outcome measures

Primary outcomes

Fetal/neonatal outcomes
1. Fetal/neonatal mortality;
2. LGA (birthweight greater than or equal to 90th percentile for gestational age);
3. macrosomia (birthweight greater than 4000 g or greater than 4500 g as defined by authors).

Maternal outcomes
1. Mode of birth (normal vaginal birth, operative vaginal birth, caesarean section).

Secondary outcomes

Fetal/neonatal outcomes
1. Neonatal hypoglycaemia requiring treatment (variously defined by authors of individual trials);
2. gestational age at birth;
3. preterm birth (less than 37 weeks' gestation);
4. birthweight;
5. small-for-gestational age;
6. shoulder dystocia;
7. bone fracture;
8. nerve palsy;
9. respiratory distress syndrome;
10. use of assisted ventilation;
11. hyperbilirubinaemia requiring treatment;
12. Apgar scores (less than seven at five minutes);
13. Apgar scores (less than four at five minutes);
14. Ponderal index*;
15. skinfold thickness measurements.

Childhood outcomes
1. Weight;
2. height;
3. body mass index (BMI);
4. fat mass/fat-free mass;
5. skinfold thickness measurements;
6. blood pressure;
7. impaired glucose tolerance (as defined by author(s));
8. type 1 diabetes;
9. type 2 diabetes;
10. insulin sensitivity (as defined by author(s));
11. dyslipidaemia or metabolic syndrome;
12. childhood neurodisability;
13. educational achievement.

Adulthood
1. Weight;
2. height;
3. BMI;
4. fat mass/fat-free mass;
5. skinfold thickness measurements;
6. blood pressure;
7. impaired glucose tolerance (as defined by author(s));
8. development of type 1 diabetes;
9. development of type 2 diabetes;
10. insulin sensitivity (as defined by author(s));
11. dyslipidaemia or metabolic syndrome;
12. educational achievement.

Maternal outcomes

Perinatal
1. Pre-eclampsia;
2. insulin or oral hypoglycaemic agent required for hyperglycaemia;
3. weight gain during pregnancy (according to IOM 2009 pregnancy weight gain guidelines);
4. induction of labour;
5. augmentation of labour;
6. perineal trauma;
7. postpartum haemorrhage;
8. postpartum infection;
9. adherence to treatment;
10. women's sense of well-being and quality of life (as defined by author(s));
11. women's view of intervention.

Childhood outcomes
1. Weight;
2. height;
3. body mass index (BMI);
4. fat mass/fat-free mass;
5. skinfold thickness measurements;
6. blood pressure;
7. impaired glucose tolerance (as defined by author(s));
8. type 1 diabetes;
9. type 2 diabetes;
10. insulin sensitivity (as defined by author(s));
11. dyslipidaemia or metabolic syndrome;
12. childhood neurodisability;
13. educational achievement.
**Long term**

1. Postnatal weight retention;
2. BMI;
3. gestational diabetes in subsequent pregnancy;
4. development of type 2 diabetes mellitus;
5. development of type 1 diabetes mellitus;
6. impaired glucose tolerance (as defined by author(s));
7. insulin sensitivity (as defined by author(s)).

**Health services cost**

1. Number of hospital visits/antenatal visits for mother;
2. dietitian visits;
3. medical physician visits;
4. cost for blood glucose monitoring during pregnancy;
5. costs to families in relation to the management provided;
6. length of postnatal stay (mother);
7. admission to neonatal nursery/neonatal intensive care unit;
8. length of postnatal stay (baby);
9. cost of maternal care;
10. cost of offspring care.

**Search methods for identification of studies**

**Electronic searches**

We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group’s Trials Register (30 September 2011).

The Cochrane Pregnancy and Childbirth Group’s Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the ‘Specialized Register’ section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We did not apply any language restrictions.

**Data collection and analysis**

**Selection of studies**

Two review authors independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We resolved disagreements through discussion and consulted a third author as necessary.

**Data extraction and management**

We designed a form to extract data. For eligible studies, at least two review authors extracted the data using the agreed form. We resolved discrepancies through discussion. We entered data into Review Manager software (RevMan 2011) and checked for accuracy.

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

**Assessment of risk of bias in included studies**

Two review authors independently assessed risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We resolved any disagreement by discussion or by involving a third assessor.

(1) Sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We assessed the method as:
- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number); or
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal the allocation sequence and determine whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We assessed the methods as:
- low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
• unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)
We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies are at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes. We assessed the methods as:
• low, high or unclear risk of bias for participants;
• low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)
We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes. We assessed methods used to blind outcome assessment as:
• low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)
We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we re-included missing data in the analyses which we undertook. We assessed methods as:
• low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
• high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; ‘as treated’ analysis done with substantial departure of intervention received from that assigned at randomisation);
• unclear risk of bias.

(5) Selective reporting bias
We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found. We assessed the methods as:
• low risk of bias (where it was clear that all of the study’s pre-specified outcomes and all expected outcomes of interest to the review had been reported);
• high risk of bias (where not all the study’s pre-specified outcomes had been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest were reported incompletely and so could not be used; study fails to include results of a key outcome that would have been expected to have been reported);
• unclear risk of bias.

(6) Other sources of bias
We described for each included study any important concerns we had about other possible sources of bias. We assessed whether each study was free of other problems that could put it at risk of bias:
• low risk of other bias;
• high risk of other bias;
• unclear whether there is risk of other bias.

(7) Overall risk of bias
We made explicit judgements about whether studies were at high risk of bias, according to the criteria given in the Handbook (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it was likely to impact on the findings. We planned to explore the impact of the level of bias through undertaking sensitivity analyses - see Sensitivity analysis.

Measures of treatment effect

Dichotomous data
For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.

Continuous data
For continuous data, we used the mean difference if outcomes were measured in the same way between trials. We used the standardised mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials
We did not identify any cluster-randomised trials for inclusion. However, if we identify cluster-randomised trial in future updates
of this review, we will include them in the analyses along with individually randomised trials. We will adjust their sample sizes using the methods described in the Handbook using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely. We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Dealing with missing data

For included studies, we noted levels of attrition. We explored the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis. For all outcomes, we carried out analyses, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses, and all participants will be analysed in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial would be the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the T², I² and Chi² statistics. We regarded heterogeneity as substantial if I² was greater than 30% and either T² was greater than zero, or there was a low P value (less than 0.10) in the Chi² test for heterogeneity.

Assessment of reporting biases

In future updates of this review, if there are 10 or more studies in the meta-analysis we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually, and use formal tests for funnel plot asymmetry. For continuous outcomes we will use the test proposed by Egger 1997, and for dichotomous outcomes we will use the test proposed by Harbord 2006. If we detect asymmetry in any of these tests or by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2011). We used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar. If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary if an average treatment effect across trials was considered clinically meaningful. We treated the random-effects summary as the average range of possible treatment effects and we discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful we would not combine trials. When we used random-effects analyses, we have presented the results as the average treatment effect with its 95% confidence interval, and the estimates of T² and P².

Subgroup analysis and investigation of heterogeneity

If we identified substantial heterogeneity, we would have investigated it using subgroup analyses and sensitivity analyses. We planned to consider whether an overall summary was meaningful, and if it was, use random-effects analysis to produce it. Different types of treatment, ways of delivering treatment, variations in the severity of hyperglycaemia and maternal characteristics may have significant effects on pregnancy outcomes. We planned to carry out the following subgroup analyses, but there were not enough trials included to conduct these subgroup analyses.

1. Maternal characteristics
   - Maternal age
     - 35 years of age or more compared with below 35 years of age.
   - Maternal body mass index (BMI) at or before trial entry
     - BMI ranges of 18.5 to 24.9 kg/m² compared with less than 18.5 kg/m²;
     - BMI ranges of 18.5 to 24.9 kg/m² compared with 25 to 29.9 kg/m²;
     - BMI ranges of 18.5 to 24.9 kg/m² compared with 30 kg/m² to 39.9 kg/m²;
     - BMI ranges of 18.5 to 24.9 kg/m² compared with 40 kg/m² or more.
   - Ethnicity
     - High-risk ethnic group compared with low risk ethnic group.
   - Parity
2. Severity of hyperglycaemia at OGTT diagnostic testing
(diagnostic criteria are defined variously by individual trials)
- All blood glucose values below diagnostic cut-off points for GDM compared with one or more values above cut-off points in diagnostic testing;
- one blood glucose value above diagnostic cut-off points for GDM compared with two values above cut-off points in diagnostic testing.

3. Types of treatment
- Dietary advice (standard dietary advice compared with individualised dietary advice);
- exercise/lifestyle intervention (standard exercise/lifestyle intervention compared with individualised exercise/lifestyle intervention);
- oral hypoglycaemics compared with insulin;
- different types of hypoglycaemics (one type of hypoglycaemics compared with another);
- different insulin regimens (one insulin regimen compared with another regimen);
- one form of treatment (e.g. dietary advice alone) compared with multiple forms of treatment (e.g. dietary and exercise advice).

4. Ways of delivering treatment
- Group intervention compared with individual intervention;
- face-to-face intervention compared with non-face-to-face intervention (e.g. phone counselling, information package, etc.).

We planned to use primary outcomes in subgroup analyses. We planned to assess differences between subgroups by interaction tests where possible.

Sensitivity analysis
We planned to carry out sensitivity analysis to explore the effects of trial quality assessed by allocation concealment and other risk of bias components, by omitting studies rated as inadequate for these components. We planned to restrict this to the primary outcomes.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search
We identified a total of 35 trials through the search of the PCG Trials Register. Following application of eligibility criteria, 24 trials were not relevant to this review due to the different study population (e.g. women with gestational diabetes mellitus (GDM), or women with normal pregnancy). We included four trials (Bevier 1999; Bonomo 2005; Grant 2011; Langer 1989) and excluded seven trials (Bung 1993; Dunne 2001; Ford 1997; Li 1987; Li 1999; Maresh 1983; Yang 2003). One trial was ongoing (Crowther 2007) and we will consider it for inclusion in the next update. We identified another ongoing trial through contacting one of the trial investigators (Wolever 2011 [pers comm]); we will also consider it for inclusion in next update. See Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Included studies
We have included four trials (involving 543 women) in this review (Bevier 1999; Bonomo 2005; Grant 2011; Langer 1989) but data from only 521 women and their babies is included in our analyses. Two of the four included studies were from the United States (Bevier 1999; Langer 1989) and one each was from Canada (Grant 2011) and Italy (Bonomo 2005).

Participants
We have included a total of 543 women in this review, and included 521 women in the data analysis. The majority of women (94%) in Bevier 1999’s study were white or of Hispanic ethnicity. One-third of women were black, Hispanic or white in Langer 1989’s study. Bonomo 2005 included only Caucasian women. Women in Grant 2011’s study were from diverse ethnicities of south east Asian, Indian, Caucasian, east Asian, Caribbean, mixed and Hispanic. Bevier 1999 and Bonomo 2005 included women with a positive 50-gram one-hour GCT but a normal 100-gram three-hour OGTT. Langer 1989 included women with a positive GCT and only one abnormal value on their 100-gram three-hour OGTT. Grant 2011 included women with a positive GCT and only one abnormal value on 75-gram two-hour OGTT. The National Diabetes Data Group GDM diagnostic criteria were used in Bevier 1999 and Langer 1989. Bonomo 2005 used Carpenter and Coustan’s criteria and Grant 2011 used Canadian Diabetes Association (CDA) criteria (details are included in Characteristics of included studies).
**Intervention and comparison**

*Bevier 1999* compared dietary counselling, home glucose monitoring and clinic random glucose check, weekly home glucose monitoring diary review with clinic random blood glucose check only. Insulin therapy was considered for women in both groups in *Bevier 1999*. In *Bonomo 2005*, interventions included dietary counselling with follow-ups to assess compliance, fortnightly checking of two-hour postprandial blood glucose, HbA1c and fructosamine at clinic, and daily urine test for ketone bodies at home; women in the control group followed standard care with no diet or pharmacological treatment (*Bonomo 2005*). All participants in *Grant 2011’s* study received diet counselling, but women in the intervention group were asked to select their starch choices from an exchange list of low glycaemic index (GI) foods, while women in the control group were asked to select their starch choices from an exchange list of intermediate- and high-GI foods, which reflected the typical dietary intake of the local population. In *Langer 1989*, interventions included capillary blood glucose monitoring seven times a day, diet counselling and insulin therapy when diet alone was not able to achieve the blood glucose target of 95 mg/dl (5.3 mmol/L); women in the control group received routine diet with baseline capillary blood glucose monitoring for four weeks (*Langer 1989*).

**Outcome**

All the four included studies focused on perinatal health related outcomes for women and their babies (*Bevier 1999; Bonomo 2005; Grant 2011; Langer 1989*). None of the included studies included longer term outcomes for mothers and their babies. See the Characteristics of included studies table for more details.

**Excluded studies**

We excluded three trials which were not randomised controlled trials (*Li 1987; Li 1999; Maresh 1983*). Two trials included women with pregnancy hyperglycaemia who had reached the diagnostic criteria for GDM (*Ford 1997; Yang 2003*). One trial used fasting plasma glucose values for pregnancy hyperglycaemia diagnosis instead of using OGTT, which did not meet the inclusion criteria for this review (*Bung 1993*). We excluded one trial as there were no published or unpublished data available (*Dunne 2001*).

**Risk of bias in included studies**

Three of the four included studies were at moderate to high risk of bias and one study (*Grant 2011*) was at low to moderate risk of bias. See Figure 1 and Figure 2.
Figure 1. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

<table>
<thead>
<tr>
<th></th>
<th>Random sequence generation (selection bias)</th>
<th>Allocation concealment (selection bias)</th>
<th>Blinding of participants and personnel (performance bias)</th>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Incomplete outcome data (attrition bias)</th>
<th>Selective reporting (reporting bias)</th>
<th>Other bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevier 1999</td>
<td>?</td>
<td>?</td>
<td>+</td>
<td>?</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Bonomo 2005</td>
<td>?</td>
<td>?</td>
<td>-</td>
<td>?</td>
<td>-</td>
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<td>+</td>
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<tr>
<td>Grant 2011</td>
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<td>?</td>
<td>+</td>
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<td>+</td>
</tr>
</tbody>
</table>
Figure 2. Risk of bias graph: review authors’ judgements about each risk of bias item presented as percentages across all included studies.

### Allocation
Three trials reported that women were randomly allocated to intervention and control groups, without information on the method of randomisation and allocation concealment (Bevier 1999; Bonomo 2005; Langer 1989). One trial (Grant 2011) used numbered, sealed, opaque envelopes to allocate women to groups, and blocks were used in sequence generation; the randomisation order in this study was generated by one of the investigators who was not involved in recruitment.

### Blinding
Grant 2011 described the trial as an “open-label” pilot study. Bonomo 2005 reported that all women and the attending physicians were informed of the results of the GCT and OGTT. Women in this trial were unlikely to be blinded; however, it was unclear about whether research personnel were blinded or not. No information on whether research personnel were blinded or not in Bevier 1999 and Langer 1989; and it is unlikely that participants were blinded in these two trials.

None of the trials reported on whether outcome assessors were blinded (Bevier 1999; Bonomo 2005; Grant 2011; Langer 1989).

### Incomplete outcome data
A total of 20 women (19.4%) were excluded post randomisation in Bevier 1999’s study. Five women (four in control group, one in experimental group) were excluded due to requiring insulin treatment; another 14 women were excluded due to poor compliance for diet and home blood glucose monitoring (HBGM) in the intervention group or receiving diet counselling and/or HBGM instruction in the control group; one woman was excluded due to therapeutic abortion (Bevier 1999).

In Bonomo 2005, there were six women (2%) in the intervention group lost to follow-up, and nine women (3%) in the intervention group and six (2%) in the control group were excluded post-randomisation due to a diagnosis of GDM during re-evaluation at 30 to 34 weeks’ gestation (Bonomo 2005).

There were no losses to follow-up or post-randomisation exclusions reported in Grant 2011 and Langer 1989.

### Selective reporting
In Bevier 1999, macrosomia was not clearly defined and the rate of macrosomia was unclear. There was no obvious risk of selective reporting in Bonomo 2005, Grant 2011 and Langer 1989.

### Other potential sources of bias
No obvious risk of other potential sources of bias for the included studies was apparent (Bevier 1999; Bonomo 2005; Grant 2011; Langer 1989).
Effects of interventions

Intensive management versus routine care

Primary outcomes

Fetal or neonatal mortality was not reported in Bevier 1999, Bonomo 2005 or Langer 1989. Grant 2011 reported that there were no fetal or neonatal deaths.

Macrosomia and LGA were reported as outcomes in all four included trials. Babies born to women in the intervention group were less likely to be LGA (three trials, 438 infants, risk ratio (RR) 0.37, 95% confidence intervals (CI) 0.20 to 0.66) (Analysis 1.1) or macroscopic (three trials, 438 infants, RR 0.38, 95% CI 0.19 to 0.74) (Analysis 1.2) when compared with those born to women in the routine care group. The overall results gave the number needed to treat of 12 (95% CI 9 to 28) for macrosomia and 10 (95% CI 7 to 17) for LGA. One trial reported results for a combined outcome of LGA or macrosomia (Bevier 1999), which suggested a significantly lower incidence of either LGA or macrosomia in the intervention group when compared with routine care group (one trial, 83 infants, RR 0.11, 95% CI 0.02 to 0.84) (Analysis 1.3).

Macrosomia was defined as birthweight at least 4000 g in Bonomo 2005 and Grant 2011. Langer 1989 reported 82% of the LGA babies were macroscopic, but the definition of macrosomia was not stated in the published paper. LGA was defined as birthweight ≥ 90th percentile in Bonomo 2005 and Langer 1989; Grant 2011 defined LGA as more than 90th percentile for sex and gestational age. In Bevier 1999, macrosomia and LGA were not clearly defined, and the results were reported as a combination of macrosomia and LGA.

For maternal primary outcomes, there were no significant differences between treatment groups in rates of caesarean section (three trials, 509 women, RR 0.93, 95% CI 0.68 to 1.27) (Analysis 1.4) or operative vaginal birth (one trial, 83 women, RR 1.37, 95% CI 0.20 to 9.27) (Analysis 1.5).

Secondary outcomes

Babies born to women in the intervention group had slightly, but statistically significant, lower birthweight when compared with those born to women in the routine care group (four trials, 521 infants, mean difference (MD) -117.33 gram, 95% CI -198.72 to -35.94) (Analysis 1.6). Results from one trial also suggested that babies in the intervention group had slightly lower Ponderal Index when compared with babies in the routine care group (one trial, 300 infants, MD -0.09; 95% CI -0.16 to -0.02) (Bonomo 2005) (Analysis 1.7). No significant differences were seen in preterm birth (two trials, 138 infants, RR 1.00; 95% CI 0.26 to 3.82) (Analysis 1.8) or gestational age at birth (four trials, 521 infants, MD -0.18; 95% CI -0.43 to 0.07) (Analysis 1.9). There was no significant difference between the two groups in terms of admission to neonatal intensive care unit (two trials, 426 infants; RR 0.64; 95% CI 0.29 to 1.45) (Analysis 1.10), small for gestational age (three trials, 509 infants, RR 1.53; 95% CI 0.81 to 2.88) (Analysis 1.11) and shoulder dystocia (one trial, 83 infants, RR 0.69; 95% CI 0.06 to 7.27) (Analysis 1.12).

Two studies reported data on neonatal hypoglycaemia and hyperbilirubinaemia (Bonomo 2005; Langer 1989). Bonomo 2005 defined neonatal hypoglycaemia as BGL below 1.7 mmol/L in any two consecutive measurements and defined hyperbilirubinaemia as plasma bilirubin at least 205 µmol/L; while Langer 1989 defined neonatal hypoglycaemia as BGL below 1.94 mmol/L and defined hyperbilirubinaemia as plasma bilirubin at least 670 µmol/L. Substantial heterogeneity was detected for neonatal hypoglycaemia (I² = 62%, T² = 1.19) and hyperbilirubinaemia (I² = 50%, T² = 0.37), hence a random-effects meta-analysis was used for each outcome. There was no significant difference seen in the incidences of hypoglycaemia (two trials, 426 infants, RR 0.39; 95% CI 0.06 to 2.54) (Analysis 1.13) and hyperbilirubinaemia (two trials, 426 infants, RR 0.79; 95% CI 0.24 to 2.60) (Analysis 1.14).

There were no data reported on other fetal or neonatal secondary outcomes, and no data reported on childhood or adulthood outcomes.

For maternal secondary outcomes, women receiving interventions were more likely to have their labour induced when compared with women receiving routine care (one trial, 83 women, RR 17.69; 95% CI 1.03 to 304.09) (Analysis 1.15). Two studies reported data on maternal weight gain; however, there was no definition on maternal weight gain given (Bonomo 2005; Langer 1989). No significant difference was seen in weight gain during pregnancy (two trials, 426 women, MD -0.63 kg; 95% CI -3.07 to 1.81, I² = 83%, T² = 2.60) (Analysis 1.16). Insulin or oral hypoglycaemic agent required for hyperglycaemia was reported in Grant 2011 with data available from 12 women, and there was no statistically significant difference between two groups (RR 1.00; 95% CI 0.30 to 3.32) (Analysis 1.17). Pre-eclampsia was only reported in Bevier 1999, and no significant difference was seen between two groups (83 women, RR 2.74; 95% CI 0.26 to 29.07) (Analysis 1.18). There were no data available on other maternal perinatal secondary outcomes and women’s longer term health outcomes.

No trials reported data on health service cost.

Subgroup analyses and sensitivity analyses

Due to the small number of studies included and limited data available, no subgroup analyses and sensitivity analyses were conducted.

DISCUSSION
Summary of main results

In this review, we found that interventions including diet counselling, blood glucose monitoring and insulin therapy for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria significantly reduced the numbers of macrosomic and LGA babies. However, these benefits may be associated with an increased use of induction of labour for the mother, possibly due to awareness of the diagnosis of pregnancy hyperglycaemia by the attending health professionals.

Overall completeness and applicability of evidence

The evidence for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria is very incomplete. The primary outcome of fetal/neonatal mortality was reported in only one pilot study (Grant 2011). There were no data available for maternal and child longer term outcomes and health service cost. With some reported secondary outcomes, including pre-eclampsia, insulin or oral hypoglycaemic agent required for hyperglycaemia, operative vaginal birth, induction of labour, shoulder dystocia, and ponderal index, evidence was based on data from a single trial.

Due to the small number of studies, moderate to high risk of bias of the included studies and small numbers of participants, the applicability of the current available evidence was limited. We have included only four small trials, with a total of 521 women and their babies in this review. All the four included trials were conducted in Western countries - Canada, Italy, and the United States.

Quality of the evidence

Three of the four included studies had moderate to high risk of bias (Bevier 1999; Bonomo 2005; Langer 1989). One study was with low risk of bias, but it accounted for limited weight in data analysis due to the small sample size of 12 women and babies.

Potential biases in the review process

The definition of the eligible population for this review may be a potential source of bias. We defined the review population as women with pregnancy hyperglycaemia not meeting gestational diabetes mellitus (GDM) and T2DM diagnostic criteria, and diagnostic criteria were defined by each individual trial. Due to the inconsistencies existing in GDM diagnosis around the world, we have included women with various degrees of pregnancy hyperglycaemia and may have included some women who could be diagnosed with GDM when using a different set of criteria.

Two of the four included trials had high risk of bias in incomplete outcome data (Bevier 1999; Bonomo 2005), which may have introduced attrition bias.

Agreements and disagreements with other studies or reviews

This review found that managing women with pregnancy hyperglycaemia not meeting GDM and T2DM diagnostic criteria was effective in reducing fetal overgrowth, without increasing the risks of instrumental birth, preterm birth, small-for-gestational age or admission to neonatal intensive care unit. These findings were inconsistent with results from large, well-designed randomised controlled trials (Crowther 2005; Landon 2009) and another Cochrane review on treatment for women with GDM (Alwan 2009).

The difference in caesarean section rate was not statistically different between the two groups in this review. Similar findings were reported in the Cochrane review (Alwan 2009) and in Crowther 2005. However, a significantly decreased caesarean section rate was found in women treated for GDM in Landon 2009. In this review, data from a single trial suggested no statistically significant difference in the rate of pre-eclampsia between women in the two groups (Bevier 1999). Different findings were reported form the previous Cochrane review (Alwan 2009) and the large randomised controlled trials on treatment for women with GDM (Crowther 2005; Landon 2009), where a reduction in the risk of pre-eclampsia was found by managing women with GDM. The disagreement may result from the limited data included in this review for this outcome measure.

Authors’ conclusions

Implications for practice

This review found interventions for women with pregnancy hyperglycaemia not meeting GDM and T2DM diagnostic criteria helped reduce the number of macrosomic and LGA babies. It is important to note that the results of this review were based on four small randomised trials with moderate to high risk of bias without follow-up outcomes for women or their babies. Until additional evidence from large well designed randomised trials becomes available, current evidence is insufficient to make conclusive suggestions on management for women with pregnancy hyperglycaemia not meeting GDM and T2DM diagnostic criteria.

Implications for research

Further larger trials with sufficient power to assess the effects of lifestyle intervention and metabolic monitoring on maternal and infant health outcomes are needed. Outcomes such as longer term...
health outcomes for women and their babies after being managed for pregnancy hyperglycaemia during pregnancy and health service cost should be included.

ACKNOWLEDGEMENTS

Thanks to Professor Thomas Wolever for providing additional information and subgroup data.

As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team) and the Group's Statistical Adviser.

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Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria (Review)

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**Metzger 2007**

**Metzger 2008**

**Morisset 2010**

**Morrison 2008**

**Mulla 2010**

**NICE 2008**

**Ornoy 2005**

**Petitt 1985**

**Petry 2010**

**Petitt 1983**

**Ragnarsdottir 2010**

**Reece 2009**

**RevMan 2011**

**Rizzo 1997**

**Rumbold 2006**

**Sacks 2009**

**Sermer 1998**

**Silva 2010**

**Silverman 1995**

**Simmons 2004**

**Slining 2010**

**Soler 1978**

**Solomon 1997**

**Stamilio 2004**

**Vohr 1997**

**Vohr 1999**

**Whincup 2008**

**WHO 1999**

**Yoge 2009**

**Zhang 2006**

* Indicates the major publication for the study
## Characteristics of included studies  [ordered by study ID]

### Bevier 1999

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>103 women with a positive 50 g 1-hour GCT (&gt; 140 mg/dl) but a negative 100 g 3-hour OGTT according to the National Diabetes Data Group (NDDG) criteria (see notes) Exclusion criteria: women with evidence of hypertension, collagen disease, chronic renal disease, cardiac or pulmonary disease, Rh sensitisation, or a history of preterm labor or SGA infants Setting: Santa Barbara, California, USA.</td>
</tr>
<tr>
<td>Interventions</td>
<td>● Women in the intervention group (n = 35) 1. Dietary counselling: 30 kcal/kg/day if woman was 80-120% of ideal body weight; or 24 kcal/kg/day if woman was greater than 120% of ideal body weight; diet consisted of 40% carbohydrate, 20% protein, and 40% fat, broken into 3 meals and 3 snacks. 2. Home blood glucose monitoring (HBGM) instruction: checking the fasting and the 1-hr postprandial BGL, using visual reagent strips. Weekly HBGM diary to clinic. 3. Weekly random BGL at clinic. 4. Weekly reinforcement of prescribed diet. 5. Insulin therapy when fasting BGL &gt; 90 mg/dl or the 1-hr BGL &gt; 120 mg/dl on 3 or more occasions. ● Women in the control group (n = 48) 1. Random BGL during regular clinic visits. 2. Insulin therapy when the random result &gt; 120 mg/dl. ● All women had haemoglobin A(_1c) (HbA(_1c)) measurement at 28 and 32 weeks.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Maternal HbA(_1c) level, pre-eclampsia, mode of birth, delivery complications (shoulder dystocia, tight nuchal cord, meconium, prolonged labor phase, abnormal fetal heart rate), gestational age at birth, Apgar score at 1 min and 5 min, birthweight, infant haemoglobin, glucose, haematocrit, morbidities, and congenital anomalies</td>
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<tr>
<td>Notes</td>
<td>● The NDDG criteria (adopted by ADA and ACOG at the time of study) 1. Fasting: &gt; 105 mg/dl (5.8 mmol/l). 2. 1-h: &gt; 190 mg/dl (10.6 mmol/l). 3. 2-h: &gt; 165 mg/dl (9.2 mmol/l). 4. 3-h: &gt; 145 mg/dl (8.1 mmol/l). 5. 2 or more of the values must be met or exceeded for GDM diagnosis.</td>
</tr>
</tbody>
</table>

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Described as women were randomly assigned to either experimental or control groups</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>No information was given on allocation concealment.</td>
</tr>
</tbody>
</table>
### Bevier 1999 (Continued)

<table>
<thead>
<tr>
<th>Blinding of participants and personnel (performance bias)</th>
<th>High risk</th>
<th>Prenatal care and deliveries were performed by six obstetricians who were not blinded to the mothers treatment group. Participants were unlikely to be blinded.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>No information on whether outcome assessors were blinded or not.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>• A total of 20 women (19.4%) were excluded post randomisation 1. 5 women (4 in control group, 1 in experimental group) required insulin. 2. 1 woman had a therapeutic abortion. 3. 14 women were noncompliant to allocated treatment (i.e. women in the intervention group did not adhere to intervention or women in the control group received diet counselling and/or home blood glucose monitoring instructions). • 83 women (45 in the control group and 35 in the intervention group) were included in analysis.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>High risk</td>
<td>There was no clear definition on macrosomia. Published data on macrosomia was unclear, and cannot be included in the meta-analysis of macrosomia.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No obvious risk of other bias.</td>
</tr>
</tbody>
</table>

### Bonomo 2005

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>300 Caucasian women with singleton pregnancies, with a positive 50 gram 1-hour GCT test ($\geq 7.8$ mmol/l) followed by a normal 100-gram OGTT according to Carpenter and Coustan's criteria (see notes) Women with one abnormal value at the 100-gram OGTT or fulfilling Carpenter and Coustan's diagnostic criteria for GDM were excluded Setting: The Diabetic and Pregnancy Centre of Niguarda Ca'Granda' Hospital in Milan, Italy</td>
</tr>
<tr>
<td>Interventions</td>
<td>• Women in the intervention group (n = 150) 1. Dietary advice providing 24-30 kcal/kg per day, based on prepregnancy body weight; caloric intake was divided into three meals and 2 or 3 snacks, and distributed as 50-55% carbohydrate, 25-30% protein, 20-25% fat. 2. Out-patient management protocol: visits every 2 weeks, when the main clinical parameters (weight, blood pressure) were recorded, discussion of dietary habits with evaluation of therapeutic compliance, and measurement of fasting and 2-h postprandial blood glucose, of HbA1c and fructosamine.</td>
</tr>
</tbody>
</table>
### Outcomes

Maternal: caesarean section; infant: gestational age at delivery, birthweight, macrosomia (birthweight $\geq 4000$ g), LGA (birthweight $\geq 90$th centile), SGA (birthweight $\leq 10$th centile), ponderal index, hypoglycaemia (any of 2 consecutive blood glucose values $< 1.7$ mmol/l), hyperbilirubinaemia (plasma values $\geq 205$ µmol/l), polycythaemia (haematocrit $> 60$%), 5-min Apgar score $< 7$, admission to neonatal intensive care unit

### Notes

- Carpenter and Coustan's diagnostic criteria
  1. Fasting: 5.3 mmol/L.
  2. 1-hour: 10.0 mmol/l.
  3. 2-hour: 8.6 mmol/l.
  4. 3-hour: 7.8 mmol/l.
  5. 2 or more results equal to or greater than the cut-off values is required for a diagnosis of GDM.
- Blood glucose targets were $< 5$ mmol/l fasting, and $< 6.7$ mmol/l 2-h postprandial for women in the intervention group.

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Described as randomly assigned to 1 of the 2 study groups, no other information available</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>No information was given on allocation concealment.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>All women, and the attending physicians were informed of the results of the GCT and OGTT. It is unclear whether research personnel are blinded from knowledge of group allocation; participants were unlikely to be blinded</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>No information on whether the outcome assessors were blinded or not</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>Losses to follow-up (2%): 6 women in the intervention group loss to follow-up. Post-randomisation exclusion (5%): 9 women in intervention group and 6 in the control group were excluded due to the diagnosis of GDM at 30-34 weeks' gestation. All those women were described as “replaced”.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No obvious risk of selective reporting.</td>
</tr>
</tbody>
</table>
Grant 2011

**Methods**
Randomised controlled pilot study.

**Participants**
12 pregnant women 18-45 years of age, diagnosed with impaired glucose tolerance of pregnancy (IGTP) according to Canadian Diabetes Association (CDA) criteria, and who had been referred to the Diabetes in Pregnancy Clinic (DIP), St. Michael's Hospital, Canada

Exclusion criteria: presence of a multiple pregnancy or an acute or chronic illness affecting carbohydrate metabolism; presence of type 1 or type 2 diabetes prior to the current pregnancy; use of insulin treatment prior to providing consent; greater than 34 weeks' gestation; and unable to communicate in English with no translator available

**Interventions**
- Women in the intervention group (n = 8): to select their starch choices from an exchange list of low glycaemic index (GI) foods.
- Women in the control group (n = 4): to select starch choices from an exchange list of intermediate- and high-GI foods, reflecting the usual intake of typical Diabetes in Pregnancy Clinic (DIP) patients.
- All women: standard medical nutrition therapy for patients with gestational diabetes followed within the DIP clinic (patients were introduced to the Diabetes Food Guide and Canadian dietary recommendations to support a healthy pregnancy. Clinic dietician recommended how many starch choices/servings each participant should consume at each meal based upon their own individual gestational energy requirements and Acceptable Macronutrient Distribution Ranges. Free-of-charge, with approximately $20/week worth of non-perishable study foods and all blood testing strips. Self-monitored blood glucose (SMBG) from baseline to week 8; 4 times/day (fasting, 2-h after breakfast, lunch and dinner); Insulin therapy if SMBG were not met with lifestyle modification within 2-3 weeks.

**Outcomes**
Primary: fasting serum glucose and HbA1c levels at baseline and 4 weeks; self-monitored blood glucose level (SMBG) from baseline to week 8
Secondary: serum glucose level, insulin, lipids and C-reactive protein at baseline and 4 weeks after intervention, maternal dietary intake, physical activity (time, type and duration), birthweight, use of insulin, macrosomia (birthweight ≥ 4000 g), LGA (> 90th percentile population specific), SGA (< 10th percentile population specific).

**Notes**
- CDA GDM diagnostic criteria
  1. Fasting: 5.3 mmol/L.
  2. 1-h 75-g OGTT: 10.6mmol/L.
  3. 2-h 75-g OGTT: 8.9mmol/L.
  4. IGTP: 1 of the values is met or exceeded.
  5. GDM: 2 of the values are met or exceeded.
Grant 2011  \textit{(Continued)}

<table>
<thead>
<tr>
<th>Random sequence generation (selection bias)</th>
<th>Unclear risk</th>
<th>Randomisation order was created by 1 of the investigators who was not involved in recruitment. It is unclear how the sequence was generated, but it is likely to be computer-generated sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Sealed, numbered, opaque envelopes were used, and various block sizes in randomisation were used</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Described as an &quot;open-label&quot; pilot study.</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>No information on whether outcome assessors were blinded.</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>2 women in the control group withdrew after randomisation, reasons given</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No obvious risk of selective reporting.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>There is no obvious risk of other bias.</td>
</tr>
</tbody>
</table>

Langer 1989

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>126 women with a positive 50 g 1-hour GCT ($\geq 130$ mg/dl) and with one abnormal value in 100 g 3-hour OGTT according to NDDG criteria Setting: Bronx, New York, USA.</td>
</tr>
<tr>
<td>Interventions</td>
<td>● Women ($n = 63$) in the intervention group 1. Capillary blood glucose monitoring: 7 times a day. 2. Diabetic management protocol: 25 kcal/kg/day for women pre-pregnancy BMI $\geq 27$ kg/m$^2$ and 30 kcal/kg/day for women pre-pregnancy BMI &lt; 27 kg/m$^2$. 3. Insulin therapy when diet alone is not able to achieve the tight glycaemic control of 95 mg/dl. The insulin dose was calculated based on 0.7 U of insulin per kg of body weight measured in pregnancy. Human insulin was administered by multiple insulin injection regimen. The standard formula for the amount of insulin prescribed was two thirds of all insulin in the morning (2:1, intermediate-acting/ regular insulin) and one third in the evening (1:1, regular/intermediate-acting).  ● Women ($n = 63$) in the control group 1. Habitual routine diet. 2. Capillary BGL monitoring for a baseline period of 4 weeks.</td>
</tr>
</tbody>
</table>
Outcomes

Maternal: gestational age at delivery, weight gain, caesarean section; hypertensive disorders
Infant: birthweight, LGA (birthweight ≥ 90th Centile); SGA (birthweight ≤ 10th centile); preterm birth (< 37 weeks’ gestation); hypoglycaemia (BGL < 35 mg/dl or 1.94 mmol/l); hyperbilirubinaemia (bilirubin > 12 mg/dl); hypocalcaemia (calcium < 7.5 mg/dl); polycythemia (central venous hematocrit > 62%); admission to neonatal intensive care unit; respiratory distress syndrome

Notes

• The NDDG criteria (adopted by ADA and ACOG at the time of study)
  1. Fasting: > 105 mg/dl (5.8 mmol/l).
  2. 1-h: > 190 mg/dl (10.6 mmol/l).
  3. 2-h: > 165 mg/dl (9.2 mmol/l).
  4. 3-h: > 145 mg/dl (8.1 mmol/l).
  5. 2 or more of the values must be met or exceeded for GDM diagnosis.
• All women were instructed to add 150 g of carbohydrate to their usual meals for each of 3 days before their 100-g OGTT.

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Described as “randomised into treated and untreated groups.”</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>No information was given on allocation concealment.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>It is unlikely to blind study participants. No information on whether research personnel was blinded or not</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>No information about whether outcome assessors were blinded.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>No loss to follow-up or post randomisation exclusion.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No obvious risk of selective reporting.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No obvious risk of other bias.</td>
</tr>
</tbody>
</table>

ACOG: American Congress of Obstetricians and Gynecologists (formerly the American College of Obstetricians and Gynecologists)
ADA: American Diabetes Association
BGL: blood glucose level
GCT: glucose challenge test
GDM: gestational diabetes mellitus
GI: glycaemic index
Characteristics of excluded studies  [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bung 1993</td>
<td>Diagnosis of “disturbed carbohydrate metabolism during pregnancy” was based on fasting plasma glucose values but not on OGTT results</td>
</tr>
<tr>
<td>Dunne 2001</td>
<td>No published or unpublished data available.</td>
</tr>
<tr>
<td>Ford 1997</td>
<td>Participants were women with GDM as defined by WHO 1980 criteria (2-hour BGL between 8 mmol/L and 11 mmol/L in 75-gram OGTT)</td>
</tr>
<tr>
<td>Li 1987</td>
<td>Participants were women with GDM according to NDDG criteria and group allocation is based on alternation</td>
</tr>
<tr>
<td>Li 1999</td>
<td>Not a randomised trial, group allocation is based on alternation</td>
</tr>
<tr>
<td>Maresh 1983</td>
<td>Not a randomised trial, group allocation by alternation.</td>
</tr>
<tr>
<td>Yang 2003</td>
<td>Participants were women with GDM according to WHO criteria (2-hour BGL between 7.8 and 11.1 mmol/L in 75-gram OGTT)</td>
</tr>
</tbody>
</table>

BGL: blood glucose level  
GDM: gestational diabetes mellitus  
NDDG: National Diabetes Data Group  
OGTT: oral glucose tolerance test

Characteristics of ongoing studies  [ordered by study ID]

Crowther 2007

<table>
<thead>
<tr>
<th>Trial name or title</th>
<th>Investigation of dietary and lifestyle advice for women with borderline gestational glucose intolerance (IDEAL study)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Randomised clinical trial.</td>
</tr>
<tr>
<td>Participants</td>
<td>Pregnant women with a singleton pregnancy, with a positive 50 g OGCT (1-h BGL ≥ 7.8 mmol/L) and a normal 2-h 75 g OGTT (fasting BGL &lt; 5.5 mmol/L and 2-h BGL &lt; 7.8 mmol/L)</td>
</tr>
<tr>
<td>Interventions</td>
<td>Lifestyle counselling (individualised diet and exercise advice from a registered dietitian based on published recommendations of the Dietitians Association of Australia), BGL monitoring and insulin therapy if necessary</td>
</tr>
</tbody>
</table>
### Crowther 2007

| Outcomes | LGA, death or serious health outcome for the infant, other causes of infant morbidity (e.g. macrosomia, SGA, neonatal hypoglycaemia requiring treatment, shoulder dystocia, nerve palsy, bone fracture, preterm birth, Apgar score < 7 at 5 minutes), serious or adverse health outcomes for the women (e.g. maternal death, pre-eclampsia, caesarean birth, induction of labour, antepartum/postpartum haemorrhage, weight gain ≥10 kg in pregnancy, need for antenatal hospitalisation), maternal psychological outcomes and health status, use of hospital services and health costs |
| Starting date | 2008. |
| Contact information | Caroline.crowther@adelaide.edu.au |
| Notes | |

### Wolever 2011 [pers comm]

| Trial name or title | |
| Methods | Randomised clinical trial. |
| Participants | Women with GDM and IGTP. |
| Interventions | Low-glycaemic index diet will be compared with control diet (intermediate- and high-glycaemic index diet) |
| Outcomes | Primary: fasting serum glucose and HbA1c levels at baseline and 4 weeks; self-monitored blood glucose level from baseline to week 8 |
| Starting date | Not yet recruiting. |
| Contact information | Thomas.wolever@utoronto.ca |
| Notes | |

BGL: blood glucose level  
GDM: gestational diabetes mellitus  
IGTP: impaired glucose tolerance of pregnancy  
LGA: large for gestational age  
OGTT: oral glucose tolerance test  
SGA: small for gestational age
### Comparison 1. Intensive management versus routine care

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Large-for-gestational age</td>
<td>3</td>
<td>438</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.37 [0.20, 0.66]</td>
</tr>
<tr>
<td>2 Macrosomia</td>
<td>3</td>
<td>438</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.38 [0.19, 0.74]</td>
</tr>
<tr>
<td>3 Large-for-gestational age or macrosomia</td>
<td>1</td>
<td>83</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.11 [0.02, 0.84]</td>
</tr>
<tr>
<td>4 Caesarean section</td>
<td>3</td>
<td></td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>4.1 Any caesarean section</td>
<td>3</td>
<td>509</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.93 [0.68, 1.27]</td>
</tr>
<tr>
<td>4.2 Primary caesarean section</td>
<td>2</td>
<td>209</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.99 [0.42, 2.33]</td>
</tr>
<tr>
<td>4.3 Repeat caesarean section</td>
<td>2</td>
<td>209</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.46 [0.17, 1.26]</td>
</tr>
<tr>
<td>5 Operative vaginal delivery</td>
<td>1</td>
<td>83</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>5.1 Unspecified</td>
<td>1</td>
<td>83</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.37 [0.20, 9.27]</td>
</tr>
<tr>
<td>5.2 Vacuum</td>
<td>1</td>
<td>83</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>2.74 [0.26, 29.07]</td>
</tr>
<tr>
<td>5.3 Forceps</td>
<td>1</td>
<td>83</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.45 [0.02, 10.82]</td>
</tr>
<tr>
<td>6 Birthweight (gram)</td>
<td>4</td>
<td>521</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-117.33 [-198.72, -35.94]</td>
</tr>
<tr>
<td>7 Ponderal index (gram x 100/m^3)</td>
<td>1</td>
<td>300</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-0.09 [-0.16, -0.02]</td>
</tr>
<tr>
<td>8 Preterm birth</td>
<td>2</td>
<td>138</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.0 [0.26, 3.82]</td>
</tr>
<tr>
<td>9 Gestational age at birth (week)</td>
<td>4</td>
<td>521</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-0.18 [-0.43, 0.07]</td>
</tr>
<tr>
<td>10 Admission to neonatal intensive care unit</td>
<td>2</td>
<td>426</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.64 [0.29, 1.45]</td>
</tr>
<tr>
<td>11 Small-for-gestational age</td>
<td>3</td>
<td>509</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.53 [0.81, 2.88]</td>
</tr>
<tr>
<td>12 Shoulder dystocia</td>
<td>1</td>
<td>83</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.69 [0.06, 7.27]</td>
</tr>
<tr>
<td>13 Neonatal hypoglycaemia</td>
<td>2</td>
<td>426</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.39 [0.06, 2.54]</td>
</tr>
<tr>
<td>14 Hyperbilirubinaemia</td>
<td>2</td>
<td>426</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.79 [0.24, 2.60]</td>
</tr>
<tr>
<td>15 Induction of labour</td>
<td>1</td>
<td>83</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>17.69 [1.03, 304.09]</td>
</tr>
<tr>
<td>16 Weight gain during pregnancy (kg)</td>
<td>2</td>
<td>426</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-0.63 [-3.07, 1.81]</td>
</tr>
<tr>
<td>17 insulin or oral hypoglycaemic agent required for hyperglycaemia</td>
<td>1</td>
<td>12</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.0 [0.30, 3.32]</td>
</tr>
<tr>
<td>18 Pre-eclampsia</td>
<td>1</td>
<td>83</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>2.74 [0.26, 29.07]</td>
</tr>
</tbody>
</table>
### Analysis 1.1. Comparison I Intensive management versus routine care, Outcome I Large-for-gestational age.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** I Intensive management versus routine care

**Outcome:** I Large-for-gestational age

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed 95% CI</td>
<td></td>
<td>M-H,Fixed 95% CI</td>
</tr>
<tr>
<td>Grant 2011</td>
<td>1/8</td>
<td>1/4</td>
<td>3.6 %</td>
<td>0.50 [0.04, 6.08]</td>
<td></td>
</tr>
<tr>
<td>Langer 1989</td>
<td>4/63</td>
<td>15/63</td>
<td>40.2 %</td>
<td>0.27 [0.09, 0.76]</td>
<td></td>
</tr>
<tr>
<td>Bonomo 2005</td>
<td>9/150</td>
<td>21/150</td>
<td>56.2 %</td>
<td>0.43 [0.20, 0.90]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>221</strong></td>
<td><strong>217</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.37 [0.20, 0.66]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 14 (Intensive care), 37 (Routine care)

Heterogeneity: $\chi^2 = 0.58$, df = 2 ($P = 0.75$); $I^2 = 0.0$

Test for overall effect: $Z = 3.35$ ($P = 0.00082$)

Test for subgroup differences: Not applicable
### Analysis 1.2. Comparison 1 Intensive management versus routine care, Outcome 2 Macrosomia.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 2 Macrosomia

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care n/N</th>
<th>Routine care n/N</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
<th>Weight M-H,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonomo 2005</td>
<td>8/150</td>
<td>16/150</td>
<td>0.50 [0.22, 1.13]</td>
<td>0.052</td>
</tr>
<tr>
<td>Grant 2011</td>
<td>0/8</td>
<td>0/4</td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
<td>Langer 1989</td>
<td>3/63</td>
<td>13/63</td>
<td>0.23 [0.07, 0.77]</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI) 221 217**

Total events: 11 (Intensive care), 29 (Routine care)

Heterogeneity: Chi² = 1.09, df = 1 (P = 0.30); I² = 8%

Test for overall effect: Z = 2.84 (P = 0.0045)

Test for subgroup differences: Not applicable

### Analysis 1.3. Comparison 1 Intensive management versus routine care, Outcome 3 Large-for-gestational age or macrosomia.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 3 Large-for-gestational age or macrosomia

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care n/N</th>
<th>Routine care n/N</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
<th>Weight M-H,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevier 1999</td>
<td>1/35</td>
<td>12/48</td>
<td>0.11 [0.02, 0.84]</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI) 35 48**

Total events: 1 (Intensive care), 12 (Routine care)

Heterogeneity: not applicable

Test for overall effect: Z = 2.13 (P = 0.033)

Test for subgroup differences: Not applicable
### Analysis 1.4. Comparison 1 Intensive management versus routine care, Outcome 4 Caesarean section.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 4 Caesarean section

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>routine care</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
<th>Weight M-H,Fixed</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**1 Any caesarean section**

- **Bevier 1999** 5/35 12/48 16.0 % 0.57 [0.22, 1.47]
- **Bonomo 2005** 44/150 42/150 66.5 % 1.05 [0.73, 1.50]
- **Langer 1989** 9/63 11/63 17.4 % 0.82 [0.36, 1.84]

**Subtotal (95% CI)** 248 261 100.0 % 0.93 [0.68, 1.27]

Total events: 58 (Intensive care), 65 (routine care)

Heterogeneity: Chi² = 1.54, df = 2 (P = 0.46); I² = 0.0%

Test for overall effect: Z = 0.45 (P = 0.65)

**2 Primary caesarean section**

- **Bevier 1999** 3/35 3/48 26.5 % 1.37 [0.29, 6.40]
- **Langer 1989** 6/63 7/63 73.5 % 0.86 [0.31, 2.41]

**Subtotal (95% CI)** 98 111 100.0 % 0.99 [0.42, 2.33]

Total events: 9 (Intensive care), 10 (routine care)

Heterogeneity: Chi² = 0.25, df = 1 (P = 0.62); I² = 0.0%

Test for overall effect: Z = 0.01 (P = 0.99)

**3 Repeat caesarean section**

- **Bevier 1999** 2/35 9/48 65.5 % 0.30 [0.07, 1.32]
- **Langer 1989** 3/63 4/63 34.5 % 0.75 [0.17, 3.22]

**Subtotal (95% CI)** 98 111 100.0 % 0.46 [0.17, 1.26]

Total events: 5 (Intensive care), 13 (routine care)

Heterogeneity: Chi² = 0.74, df = 1 (P = 0.39); I² = 0.0%

Test for overall effect: Z = 1.51 (P = 0.13)

Test for subgroup differences: Chi² = 1.79, df = 2 (P = 0.41); I² = 0.0%
## Analysis 1.5. Comparison 1 Intensive management versus routine care, Outcome 5 Operative vaginal delivery.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 5 Operative vaginal delivery

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
</tr>
<tr>
<td>1 Unspecified</td>
<td>2/35</td>
<td>2/48</td>
<td>1.37 [0.20, 9.27]</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>35</td>
<td>48</td>
<td>1.37 [0.20, 9.27]</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Vacuum</td>
<td>2/35</td>
<td>1/48</td>
<td>2.74 [0.26, 29.07]</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>35</td>
<td>48</td>
<td>2.74 [0.26, 29.07]</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Forceps</td>
<td>0/35</td>
<td>1/48</td>
<td>0.45 [0.02, 10.82]</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>35</td>
<td>48</td>
<td>0.45 [0.02, 10.82]</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 0.32 (P = 0.75)

Test for subgroup differences: Chi² = 0.80, df = 2 (P = 0.67), I² = 0.0%

Favours intensive care  Favours routine care
Analysis 1.6. Comparison 1 Intensive management versus routine care, Outcome 6 Birthweight (gram).

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 6 Birthweight (gram)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevier 1999</td>
<td>35 3311 (459)</td>
<td>48 3600 (511)</td>
<td></td>
<td>15.0 %</td>
<td>-289.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bonomo 2005</td>
<td>150 3365 (436)</td>
<td>150 3436.6 (462)</td>
<td></td>
<td>64.1 %</td>
<td>-71.60</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grant 2011</td>
<td>8 3334 (353)</td>
<td>4 3256 (480)</td>
<td></td>
<td>2.4 %</td>
<td>78.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Langer 1989</td>
<td>63 3261 (496)</td>
<td>63 3422 (384)</td>
<td></td>
<td>18.5 %</td>
<td>-161.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>256</td>
<td>265</td>
<td></td>
<td>100.0 %</td>
<td>-117.33</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi^2 = 4.08, df = 3 (P = 0.25); I^2 = 26%
Test for overall effect: Z = 2.83 (P = 0.0047)
Test for subgroup differences: Not applicable

Analysis 1.7. Comparison 1 Intensive management versus routine care, Outcome 7 Ponderal index (gram x 100/m^3).

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 7 Ponderal index (gram x 100/m^3)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonomo 2005</td>
<td>150 2.64 (0.24)</td>
<td>150 2.73 (0.35)</td>
<td></td>
<td>100.0 %</td>
<td>-0.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>150</td>
<td>150</td>
<td></td>
<td>100.0 %</td>
<td>-0.09</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable
Test for overall effect: Z = 2.60 (P = 0.0094)
Test for subgroup differences: Not applicable

Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria (Review) 34
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Analysis 1.8. Comparison 1 Intensive management versus routine care, Outcome 8 Preterm birth.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 8 Preterm birth

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H, Fixed</td>
<td>95% CI</td>
<td>M-H, Fixed</td>
</tr>
<tr>
<td>Grant 2011</td>
<td>0/8</td>
<td>0/4</td>
<td>Not estimable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Langer 1989</td>
<td>4/63</td>
<td>4/63</td>
<td>100.0 %</td>
<td>1.00 [ 0.26, 3.82 ]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>71</td>
<td>67</td>
<td>100.0 %</td>
<td>1.00 [ 0.26, 3.82 ]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 4 (Intensive care), 4 (Routine care)

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P = 1.0)

Test for subgroup differences: Not applicable
### Analysis 1.9. Comparison 1 Intensive management versus routine care, Outcome 9 Gestational age at birth (week).

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria.

Comparison: 1 Intensive management versus routine care.

Outcome: 9 Gestational age at birth (week).

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Weight</th>
<th>Mean Difference IV,Fixed,95% CI</th>
<th>Mean Difference IV,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N  Mean(SD)</td>
<td>N  Mean(SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bevier 1999</td>
<td>35  39.4 (1.5)</td>
<td>48  39.6 (1.3)</td>
<td>16.4 %</td>
<td>-0.20 [-0.82, 0.42]</td>
<td></td>
</tr>
<tr>
<td>Bonomo 2005</td>
<td>150 39.4 (1.2)</td>
<td>150 39.6 (1.7)</td>
<td>56.4 %</td>
<td>-0.20 [-0.53, 0.13]</td>
<td></td>
</tr>
<tr>
<td>Grant 2011</td>
<td>8  38.3 (1.2)</td>
<td>4  38.8 (0.5)</td>
<td>6.7 %</td>
<td>-0.50 [-1.47, 0.47]</td>
<td></td>
</tr>
<tr>
<td>Langer 1989</td>
<td>63  39 (2)</td>
<td>63  39 (1)</td>
<td>20.5 %</td>
<td>0.0 [-0.55, 0.55]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>256</strong></td>
<td><strong>265</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>-0.18 [-0.43, 0.07]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 0.85, df = 3 (P = 0.84); I² = 0.0%
Test for overall effect: Z = 1.40 (P = 0.16)
Test for subgroup differences: Not applicable

Heterogeneity: Chi² = 0.85, df = 3 (P = 0.84); I² = 0.0%
Test for overall effect: Z = 1.40 (P = 0.16)
Test for subgroup differences: Not applicable

---

*Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria (Review)*

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### Analysis 1.10. Comparison 1 Intensive management versus routine care, Outcome 10 Admission to neonatal intensive care unit.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 10 Admission to neonatal intensive care unit

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonomo 2005</td>
<td>5/150</td>
<td>7/150</td>
<td>0.71 [ 0.23, 2.20 ]</td>
<td>50.0 %</td>
<td></td>
</tr>
<tr>
<td>Langer 1989</td>
<td>4/63</td>
<td>7/63</td>
<td>0.57 [ 0.18, 1.86 ]</td>
<td>50.0 %</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI)**: 213 213

Total events: 9 (Intensive care), 14 (Routine care)

Heterogeneity: Chi^2 = 0.07, df = 1 (P = 0.79); I^2 =0.0%

Test for overall effect: Z = 1.07 (P = 0.29)

Test for subgroup differences: Not applicable

### Analysis 1.11. Comparison 1 Intensive management versus routine care, Outcome 11 Small-for-gestational age.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 11 Small-for-gestational age

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevier 1999</td>
<td>3/35</td>
<td>2/48</td>
<td>2.06 [ 0.36, 11.67 ]</td>
<td>11.5 %</td>
<td></td>
</tr>
<tr>
<td>Bonomo 2005</td>
<td>13/150</td>
<td>9/150</td>
<td>1.44 [ 0.64, 3.28 ]</td>
<td>61.3 %</td>
<td></td>
</tr>
<tr>
<td>Langer 1989</td>
<td>6/63</td>
<td>4/63</td>
<td>1.50 [ 0.44, 5.06 ]</td>
<td>27.2 %</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI)**: 248 261

Total events: 22 (Intensive care), 15 (Routine care)

Heterogeneity: Chi^2 = 0.13, df = 2 (P = 0.94); I^2 =0.0%

Test for overall effect: Z = 1.32 (P = 0.19)

Test for subgroup differences: Not applicable
**Analysis 1.12. Comparison 1 Intensive management versus routine care, Outcome 12 Shoulder dystocia.**

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 12 Shoulder dystocia

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
</tr>
<tr>
<td>Bevier 1999</td>
<td>1/35</td>
<td>2/48</td>
<td>100.0 %</td>
<td>0.69 [ 0.06, 7.27 ]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>35</strong></td>
<td><strong>48</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.69 [ 0.06, 7.27 ]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 1 (Intensive care), 2 (Routine care)

Heterogeneity: not applicable

Test for overall effect: Z = 0.31 (P = 0.75)

Test for subgroup differences: Not applicable
### Analysis 1.13. Comparison 1 Intensive management versus routine care, Outcome 13 Neonatal hypoglycaemia.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 13 Neonatal hypoglycaemia

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bonomo 2005</td>
<td>5/150</td>
<td>6/150</td>
<td></td>
<td>59.7%</td>
<td>0.83 [0.26, 2.67]</td>
</tr>
<tr>
<td>Langer 1989</td>
<td>1/63</td>
<td>8/63</td>
<td></td>
<td>40.3%</td>
<td>0.13 [0.02, 0.97]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>213</strong></td>
<td><strong>213</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>0.39 [0.06, 2.54]</strong></td>
</tr>
</tbody>
</table>

Total events: 6 (Intensive care), 14 (Routine care)

### Analysis 1.14. Comparison 1 Intensive management versus routine care, Outcome 14 Hyperbilirubinaemia.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 14 Hyperbilirubinaemia

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bonomo 2005</td>
<td>6/150</td>
<td>4/150</td>
<td>47.5%</td>
<td>1.50 [0.43, 5.21]</td>
<td></td>
</tr>
<tr>
<td>Langer 1989</td>
<td>4/63</td>
<td>9/63</td>
<td>52.5%</td>
<td>0.44 [0.14, 1.37]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>213</strong></td>
<td><strong>213</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>0.79 [0.24, 2.60]</strong></td>
</tr>
</tbody>
</table>

Total events: 10 (Intensive care), 13 (Routine care)

Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria (Review)
### Analysis 1.15. Comparison 1 Intensive management versus routine care, Outcome 15 Induction of labour.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 15 Induction of labour

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed(95% CI)</td>
<td></td>
<td>M-H,Fixed(95% CI)</td>
</tr>
<tr>
<td>Bevier 1999</td>
<td>6/35</td>
<td>0/48</td>
<td>100.0 %</td>
<td>17.69 [ 1.03, 304.09 ]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>35</strong></td>
<td><strong>48</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>17.69 [ 1.03, 304.09 ]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 6 (Intensive care), 0 (Routine care)

Heterogeneity: not applicable

Test for overall effect: Z = 1.98 (P = 0.048)

Test for subgroup differences: Not applicable

---

*Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria (Review)*

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### Analysis 1.16. Comparison 1 Intensive management versus routine care, Outcome 16 Weight gain during pregnancy (kg).

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 16 Weight gain during pregnancy (kg)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Mean Difference</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV(Random,95% CI)</td>
</tr>
<tr>
<td>Bonomo 2005</td>
<td>150 13.1 (4.3)</td>
<td>150 12.6 (3.9)</td>
<td>0.50 [-0.43, 1.43]</td>
<td></td>
</tr>
<tr>
<td>Langer 1989</td>
<td>63 13 (4)</td>
<td>63 15 (6)</td>
<td>-2.00 [-3.78, -0.22]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>213</td>
<td>213</td>
<td>-0.63 [-3.07, 1.81]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 2.60; \ Chi^2 = 5.95, df = 1 (P = 0.01);$ $I^2 = 83\%$

Test for overall effect: $Z = 0.51 (P = 0.61)$

Test for subgroup differences: Not applicable

---

### Analysis 1.17. Comparison 1 Intensive management versus routine care, Outcome 17 insulin or oral hypoglycaemic agent required for hyperglycaemia.

**Review:** Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

**Comparison:** 1 Intensive management versus routine care

**Outcome:** 17 insulin or oral hypoglycaemic agent required for hyperglycaemia

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
</tr>
<tr>
<td>Grant 2011</td>
<td>4/8</td>
<td>2/4</td>
<td>100.0 %</td>
<td>1.00 [ 0.30, 3.32 ]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>8</td>
<td>4</td>
<td>100.0 %</td>
<td>1.00 [ 0.30, 3.32 ]</td>
</tr>
</tbody>
</table>

Total events: 4 (Intensive care), 2 (Routine care)

Heterogeneity: not applicable

Test for overall effect: $Z = 0.00 (P = 1.0)$

Test for subgroup differences: Not applicable

---

*Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria (Review)*

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Analysis 1.18. Comparison 1 Intensive management versus routine care, Outcome 18 Pre-eclampsia.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 18 Pre-eclampsia

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intensive care</th>
<th>Routine care</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevior 1999</td>
<td>2/35</td>
<td>1/48</td>
<td>100.0 %</td>
<td>2.74 [0.26, 29.07]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td><strong>35</strong></td>
<td><strong>48</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>2.74 [0.26, 29.07]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 2 (Intensive care), 1 (Routine care)
Heterogeneity: not applicable
Test for overall effect: Z = 0.84 (P = 0.40)
Test for subgroup differences: Not applicable

WHAT’S NEW
Last assessed as up-to-date: 21 November 2011.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 April 2012</td>
<td>Amended</td>
<td>Corrected typographical error in Agreements and disagreements with other studies or reviews.</td>
</tr>
</tbody>
</table>

HISTORY
Review first published: Issue 1, 2012

CONTRIBUTIONS OF AUTHORS
Shanshan Han wrote drafts of the protocol and review, with Caroline Crowther and Philippa Middleton contributing to data extraction, and commenting on and editing to all drafts.
DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

• ARCH, Robinson Institute, The University of Adelaide, Australia.

External sources

• Australian Department of Health and Ageing, Australia.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

A combined outcome of ‘large-for-gestational age or macrosomia’ was added in the review.

INDEX TERMS

Medical Subject Headings (MeSH)

Blood Glucose [analysis]; Cesarean Section [utilization]; Diabetes Mellitus, Type 2 [blood; *diagnosis]; Diabetes, Gestational [blood; *diagnosis]; Fetal Macrosomia [prevention & control]; Glucose Tolerance Test; Hyperglycemia [diet therapy; *therapy]; Hypoglycemic Agents [therapeutic use]; Infant, Newborn; Infant, Postmature; Insulin [therapeutic use]; Patient Education as Topic; Pregnancy Complications [blood; diet therapy; *therapy]; Pregnant Women; Publication Bias; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Pregnancy