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[Intervention Review]

Treatments for gestational diabetes

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ABSTRACT

Background

Gestational diabetes (GDM) affects 3% to 6% of all pregnancies. Women are often intensively managed with increased obstetric monitoring, dietary regulation, and insulin. However, there has been no sound evidence base to support intensive treatment. The key issue for clinicians and consumers is whether treatment of GDM improves perinatal outcome.

Objectives

To compare the effect of alternative treatment policies for GDM on both maternal and infant outcomes.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (January 2009) and bibliographies of relevant papers. We updated this search on 1 July 2011 and added the results to the awaiting classification section of the review.

Selection criteria

Randomised controlled trials comparing alternative management strategies for women with GDM and impaired glucose tolerance in pregnancy.

Data collection and analysis

Two authors and a member of the Cochrane Pregnancy and Childbirth Group's editorial team extracted and checked data independently. Disagreements were resolved through discussion with the third author.

Main results

Eight randomised controlled trials (1418 women) were included.

Caesarean section rate was not significantly different when comparing any specific treatment with routine antenatal care (ANC) including data from five trials with 1255 participants (risk ratio (RR) 0.94, 95% confidence interval (CI) 0.80 to 1.12). However, when comparing oral hypoglycaemics with insulin as treatment for GDM, there was a significant reduction (RR 0.46, 95% CI 0.27 to 0.77, two trials, 90 participants).

There was a reduction in the risk of pre-eclampsia with intensive treatment (including dietary advice and insulin) compared to routine ANC (RR 0.65, 95% CI 0.48 to 0.88, one trial, 1000 participants). More women had their labours induced when given specific treatment compared to routine ANC (RR 1.33, 95% CI 1.13 to 1.57, two trials, 1068 participants). The composite outcome of perinatal morbidity (death,

shoulder dystocia, bone fracture and nerve palsy) was significantly reduced for those receiving intensive treatment for mild GDM compared to routine ANC (RR 0.32, 95% CI 0.14 to 0.73, one trial, 1030 infants).

There was a reduction in the proportion of infants weighing more than 4000 grams (RR 0.46, 95% CI 0.34 to 0.63, one trial, 1030 infants) and the proportion of infants weighing greater than the 90th birth centile (RR 0.55, 95% CI 0.30 to 0.99, three trials, 223 infants) of mothers receiving specific treatment for GDM compared to routine ANC. However, there was no statistically significant difference in this proportion between infants of mothers receiving oral drugs compared to insulin as treatment for GDM.

Authors' conclusions

Specific treatment including dietary advice and insulin for mild GDM reduces the risk of maternal and perinatal morbidity. However, it is associated with higher risk of labour induction. More research is needed to assess the impact of different types of intensive treatment, including oral drugs and insulin, on individual short- and long-term infant outcomes.

[Note: the 29 citations in the awaiting classification section of the review may alter the conclusions of the review once assessed.]

PLAIN LANGUAGE SUMMARY

Treatments for gestational diabetes

The best way of identifying and treating women with abnormal blood glucose tests in pregnancy is not known. Raised blood glucose levels during pregnancy is known as gestational diabetes. This abnormality may be associated with bigger babies, more difficult births and could be associated with higher rates of operative delivery such as caesarean section. The review of eight studies (1418 women) suggests that offering specific treatment for gestational diabetes may be associated with better baby and mother outcomes, but has not found robust evidence on the best choice of treatment which provides the better outcomes for these women and their babies, even if identified correctly. More research is needed to assess long-term mother and baby outcomes.

BACKGROUND

Metabolic changes during pregnancy lower glucose tolerance. Blood glucose levels rise and more insulin is produced in response. As the pregnancy develops, insulin demands increase. For the majority of pregnant women this is a normal physiological process. However, some women develop glucose intolerance resulting in gestational diabetes affecting between 3% and 6% of all pregnancies (Gabbe 1977). Women who had diabetes before becoming pregnant (pre-existing diabetes) can see their insulin requirements progressively rise throughout pregnancy.

Definition and diagnosis of gestational diabetes (GDM)

GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. The definition applies regardless of whether insulin or only diet modification is used for treatment or whether the condition persists after pregnancy. It does not exclude the possibility that unrecognised glucose intolerance may have antedated or begun concomitantly with the pregnancy (Expert Committee 2003).

The diagnosis is generally based on an abnormal oral glucose tolerance test (GTT). A GTT requires women to fast overnight before attending the hospital the following morning. Usually, two blood samples are taken. The first is taken on arrival and the woman is then given a sugary drink containing 75 g of glucose (100 g is more commonly used in the United States). The second blood sample is taken two hours later. The precise diagnostic values of the GTT are controversial (Weiss 1998), making it difficult to provide a clear definition of gestational diabetes. Previously, two distinct diagnostic categories existed; impaired glucose tolerance (IGT) and GDM. However, current World Health Organization recommendations suggest that all abnormal glucose metabolism arising in pregnancy should be defined as gestational diabetes (Alberti 1998). The new National Institute for Clinical Excellence (NICE) Guidelines use the WHO criteria (NICE 2007). However, this does not distinguish between mild and more severe abnormalities of glucose tolerance. Although it has been suggested that the relationship between blood glucose levels in pregnancy and perinatal outcome is a continuous one and no single cut off can separate women into those with high risk and those with no risk at all (Coustan 1998), it is helpful to classify GDM into mild and severe forms (see 'Methods' section).

This review defines gestational diabetes according to the following values:

- fasting blood glucose greater than 7 mmol/l; or
- two-hour blood glucose greater than 7.8 mmol/l following a 75 g GTT.

In the USA a 100 g glucose load is commonly used and there is some debate around the precise diagnostic values. This review accepted clearly defined values as described by the American College of Obstetricians and Gynaecologists:

- gestational diabetes - fasting greater than 105 mg/dl; one-hour greater than 190 mg/dl; two-hour greater than 165 mg/dl; three-hour greater than 145 mg/dl.

Screening for gestational diabetes

There are various regimens that are used to select women for formal testing with a GTT (Stephenson 1993). Examples of these are a past history of gestational diabetes or IGT, the development of pregnancy complications such as polyhydramnios (increased water around the baby) or a raised random blood glucose. In addition, there are certain predisposing factors which may indicate an increased risk of gestational diabetes such as obesity and ethnicity (Essel 1995). Inevitably, some women diagnosed in pregnancy will have developed true diabetes and women with gestational diabetes should have a postnatal GTT. However, the focus of this review is abnormalities of glucose tolerance associated with pregnancy.

In the past it was pointed out that there was little evidence to support the recommendation that all pregnant women should be screened for gestational diabetes (Enkin 2000). This issue remains controversial. A systematic review of screening for gestational diabetes concluded there was insufficient evidence to justify universal screening (Scott 2002), and a protocol for a Cochrane review of screening for gestational diabetes has been developed (Tieu 2008b). Justification for screening rests on the relevance of gestational diabetes which remains uncertain. The key issue is whether treatment improves outcome or, more importantly, whether treatment is associated with adverse outcome.

Complications of gestational diabetes

Whilst it is recognised that women with pre-existing diabetes have an increased risk of both maternal and fetal complications (Enkin 2000) including caesarean section, hypoglycaemia, respiratory distress syndrome and stillbirth, there are currently limited data available on the frequency of adverse perinatal outcome resulting from gestational diabetes. The lack of evidence fuels confusion and leads clinicians to conclude that the risk of adverse perinatal outcome is equal to that of pre-existing diabetes.

The only commonly reported complication of gestational diabetes is macrosomia (birthweight greater than 4000 g) which may increase the risk of caesarean section, shoulder dystocia and birth trauma to the baby (Jarrett 1997). Increased birthweight is indeed associated with increased morbidity (Scott 2002). However, the association between abnormalities of glucose tolerance and increased birthweight remains unclear. It has been suggested that fetal growth acceleration associated with gestational diabetes can be corrected with dietary regulation and insulin (Soares 1997) and there may be long-term benefits to infants of normalising birthweight (Barker 1992). However, some studies suggest that macrosomia is more closely related to maternal weight or maternal weight gain than blood glucose levels (Green 1991; Essel 1995; Spellacy 1985). Furthermore, there are inconsistencies in defining macrosomia. It is suggested that there may be a continuum of risk in relation to glucose values making dichotomous cut-off values inappropriate (Scott 2002).

A further consideration is the long-term consequences for the mother. Women with gestational diabetes may have an increased risk of progression to non-insulin dependent diabetes in later life, although this is influenced greatly by, again, maternal weight and also ethnicity (Soares 1997).

Current management policies

There has been much confusion surrounding the management of gestational diabetes. Many women are managed according to intensive treatment regimens, including administration of insulin, in the belief that this will prevent pregnancy complications. The rationale being to reduce blood glucose levels in the belief that this will improve maternal and infant outcomes. Interventions include dietary regulation, home blood glucose monitoring and in some cases insulin therapy. Exercise has been suggested as an alternative and less invasive intervention and is now the subject of a Cochrane review (Ceysens 2006). Another Cochrane review assesses the impact of dietary advice on the prevention of GDM (Tieu 2008a). Increased obstetric monitoring often becomes inevitable in the form of more frequent antenatal clinic visits and ultrasound scans which intend to detect abnormalities and avoid macrosomia and stillbirth. However, they also result in an increased level of inconvenience for women compared with standard antenatal care. Furthermore, a diagnosis of gestational diabetes may cause distress in someone who previously thought herself to be healthy (Jarrett 1997).

Rationale for this review

The key issue for both clinicians and consumers is whether identification and treatment of gestational diabetes will improve perinatal outcome, particularly in the case of mild GDM. There is almost clinical consensus to treat severe forms of GDM. However, treating the milder forms of GDM is more controversial; therefore, most of the randomised controlled trials in this area have been done to examine the effect of treatment on mild GDM (previously known as IGT). This review includes the complete range of management options for gestational diabetes from no specific treatment to intensive treatment including individualised dietary advice, close monitoring of blood glucose, insulin therapy and oral hypoglycaemic drugs.

OBJECTIVES

To conduct a systematic review of randomised trials, comparing alternative treatment options for women with gestational diabetes and their effect on maternal and infant outcomes.

METHODS

Criteria for considering studies for this review

Types of studies

All published and unpublished randomised controlled trials comparing alternative management strategies for women with gestational diabetes. Quasi-random designs were excluded.

Types of participants

Pregnant women diagnosed with gestational diabetes mellitus (GDM) or impaired glucose tolerance (IGT) identified by a 75 g or 100 g oral glucose tolerance test (GTT). Studies without a formal GTT were only considered where a fasting blood glucose value greater than seven was used for diagnosis. Women were eligible irrespective of gestation and whether singleton or multiple pregnancy; however, women with pre-existing diabetes were not.

GDM was defined as fasting blood glucose of at least 7.0 mmol/L or two-hour blood glucose greater than 7.8 mmol/L. This includes

IGT which is defined as two-hour value between 7.8 mmol/L and 11 mmol/L. Participants with IGT values between 7.8 to 11 mmol/L are classified as having mild GDM. IGT values greater than 11 mmol/L are classified as severe GDM.

Types of interventions

Interventions include any form of management of gestational diabetes on top of routine antenatal care (ANC). These include any form of dietary advice (standard or specific); and drug treatment including insulin and oral drugs. One form of management can be compared to routine ANC, or two forms of management can be compared against each other. Trials that compare two or more types of the same form of treatment (oral drugs or insulin) against each other are not considered in this review.

Types of outcome measures

Maternal outcomes

- Risk of operative abdominal operative delivery.
- Risk of vaginal operative delivery.
- Psychological impact of treatment (assessed by psychometric testing).
- Levels of maternal inconvenience assessed by number of hospital visits, number of days in hospital (antenatal), extra investigations, antenatal tests (ultrasound scanning, cardiotocographs, amniocentesis), duration of antenatal admission.
- Risk of induction of labour.
- Use of insulin.
- Risk of pre-eclampsia.
- Risk of abruption.
- Risk of postpartum haemorrhage.
- Risk of third degree tears.
- Risk of postpartum infection.
- Risk of postnatal depression.
- Risk of hypoglycaemic events.
- Risk of future non-insulin dependent diabetes mellitus.

Infant outcomes

- Perinatal death.
- Birthweight greater than 90th centile, birthweight greater than 4000 g, and birthweight as a continuous variable.
- Gestation at delivery.
- Risk of shoulder dystocia (defined as halt to spontaneous delivery because the baby's shoulder is wedged behind the mother's pubis).
- Risk of birth trauma.
- Risk of nerve palsy or fracture, or both.
- Admission to neonatal intensive care unit or special care baby unit and length of stay.
- Risk of respiratory distress syndrome and ventilation.
- Hypoglycaemia and risk of neonatal infection.
- Growth and development.
- Adiposity.
- Composite outcome (defined as one or more of the following: infant death, shoulder dystocia, bone fracture and nerve palsy). Although this outcome was not included in the original protocol

for the review, it has been added as it is the primary outcome used by the ACHOIS trial (Crowther 2005), which includes the biggest sample among all the other studies included in this review.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (January 2009). We updated this search on 1 July 2011 and added the results to [Studies awaiting classification](#).

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.

For additional searching carried out for the previous version of the review, please see [Appendix 1](#).

Searching other resources

We searched bibliographies of relevant papers.

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

We assessed for inclusion all potential studies we identified as a result of the search. We resolved any disagreement through discussion.

Assessment of methodological quality of included studies

We assessed the validity of each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2005). Methods used for generation of the randomisation sequence are described for each trial.

(1) Selection bias (allocation concealment)

We assigned a quality score for each trial, using the following criteria:

- (A) adequate concealment of allocation: such as telephone randomisation, consecutively numbered sealed opaque envelopes;
- (B) unclear whether adequate concealment of allocation: such as list or table used, sealed envelopes, or study does not report any concealment approach;
- (C) inadequate concealment of allocation: such as open list of random-number tables, use of case record numbers, dates of birth or days of the week.

(2) Attrition bias (loss of participants, e.g. withdrawals, dropouts, protocol deviations)

We assessed completeness to follow up using the following criteria:

- (A) less than 5% loss of participants (10% for long-term outcomes);
- (B) 5% to 9.9% loss of participants (10% to 19.9% for long-term outcomes);
- (C) 10% to 19.9% loss of participants (20% to 39.9% for long-term outcomes);
- (D) more than 20% loss of participants (40% for long-term outcomes).

Long-term outcomes are defined as those needing follow up for more than one year.

If attrition bias scored D using the above criteria, data were not used in the main analysis of the review.

(3) Performance bias (blinding of participants, researchers and outcome assessment)

We assessed blinding using the following criteria:

- (A) blinding of participants (yes/no/unclear);
- (B) blinding of caregiver (yes/no/unclear);
- (C) blinding of outcome assessment (yes/no/unclear).

Data extraction and management

At least two review authors extracted the data using the agreed form. We resolved discrepancies through discussion. We used the Review Manager software (RevMan 2003) to double enter all the data.

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

Measures of treatment effect

We carried out statistical analysis using the Review Manager software (RevMan 2003). We used fixed-effect meta-analysis for combining data in the absence of significant heterogeneity if trials are sufficiently similar.

Dichotomous data

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

Continuous data

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

Available case analysis

We have analysed data on all participants with available data in the group to which they are allocated, regardless of whether or not they received the allocated intervention. If in the original reports participants were not analysed in the group to which they were randomised, and there was sufficient information in the trial report, we have attempted to restore them to the correct group.

Assessment of heterogeneity

We have applied tests of heterogeneity between trials, if appropriate, using the I^2 statistic. A random-effects meta-analysis is used as an overall summary if was considered appropriate.

Subgroup analyses

We performed subgroup analyses by:

- type of treatment;
- severity of GDM.

Sensitivity analyses

We carried out sensitivity analysis to explore the effect of trial quality assessed by concealment of allocation, by excluding studies with clearly inadequate allocation of concealment (rated C).

RESULTS

Description of studies

Included studies

The search identified 65 trials; eight are included in the review, involving 1418 women and their babies, and 57 excluded. Of the trials included, the majority were small with the exception of [Crowther 2005](#) (The ACHOIS trial), which randomised 1000 women to either care in which universal screening and treatment of GDM was available or care in which universal screening for GDM was not available. The sample size for the other studies ranged from 32 to 126.

Study interventions

Each study addressed treatments for gestational diabetes. Diagnosis was made either by 75 g or 100 g oral glucose tolerance test. The trials compared different interventions. Three trials compared oral hypoglycaemics to insulin treatment ([Bertini 2005](#); [Hague 2003](#); [Moore 2004](#)). [Bancroft 2000](#) compared regular capillary glucose monitoring and fetal growth monitoring, dietary advice and insulin treatment to routine care including standard dietary advice. One study compared specific "diabetic type" dietary advice to standard care ([Ford 1997](#)). One study compared specific advice for targeted intake of foods rich in unsaturated fats compared to "diabetic type" dietary advice ([Gillen 2004](#)).

Interventions used in the included trials included:

1. dietary advice, monthly HBA1c, capillary glucose monitoring and insulin therapy if indicated ([Bancroft 2000](#));
2. universal screening for GDM, individualised dietary advice from qualified dietician, glucose self monitoring, and insulin therapy if indicated ([Crowther 2005](#));
3. specific "diabetic type" dietary advice ([Ford 1997](#));

4. dietary advice for targeted intakes of foods rich in unsaturated fats ([Gillen 2004](#));
5. metformin versus insulin ([Hague 2003](#); [Moore 2004](#));
6. glyberide versus insulin ([Bertini 2005](#));
7. acarbose versus insulin ([Bertini 2005](#));
8. diabetic protocol including dietary advice and insulin therapy if indicated ([Langer 1989](#)).

Excluded studies

Many well known and influential studies were excluded from this review. Some were excluded as a consequence of methodological issues. Many were excluded due to the variation in diagnostic criteria which rendered attempts to synthesise data impossible. Others were excluded as they contained an additional screening step that selected from within the population of gestational diabetes.

(Nineteen reports from an updated search in 1 July 2011 have been added to [Studies awaiting classification](#).)

Risk of bias in included studies

All included studies stated that women were randomly allocated to intervention or control groups. Information regarding generation of the randomisation sequence was clearly described in five studies. Of these, three trials used computerised randomisation ([Bancroft 2000](#); [Crowther 2005](#); [Langer 1989](#)). Randomisation was achieved with random-number tables in one study ([Gillen 2004](#)), random selection of sealed envelopes was used in two studies ([Ford 1997](#); [Moore 2004](#)). Two trials stated women 'were randomised' ([Bertini 2005](#); [Hague 2003](#)).

Allocation concealment was adequately described in four trials ([Bancroft 2000](#); [Crowther 2005](#); [Ford 1997](#); [Langer 1989](#)). One other trial ([Moore 2004](#)) used sealed envelopes that were not described as opaque (classified as B - unclear). One trial ([Gillen 2004](#)) used an open table of random numbers (classified C - inadequate). The remaining trials ([Hague 2003](#); [Bertini 2005](#)) gave no information.

Blinding of clinician was stated for two trials ([Bancroft 2000](#); [Crowther 2005](#)), of participant for one trial ([Gillen 2004](#)), and of outcome assessor for one trial ([Crowther 2005](#)).

A number of outcomes are only reported by one trial and many of the outcomes are not addressed by any of the included studies.

Effects of interventions

Eight trials, involving 1418 women, were included in this review.

Comparison one: any specific treatment versus routine antenatal care (ANC)(subgroups by type of specific treatment)

Maternal outcomes

There was a reduction in the risk of pre-eclampsia with specific treatment for GDM compared to routine ANC (one trial, 1000 women; risk ratio (RR) 0.65, 95% confidence interval (CI) 0.48 to 0.88).

The difference in caesarean section rates was not statistically significant between the two groups (five trials, 1255 women; RR 0.95, 95% CI 0.80 to 1.12). However, women who received specific treatment were more likely to have their labour induced compared

to women who received routine ANC only (two trials, 1068 women; RR 1.33, 95% CI 1.13 to 1.57).

There were no statistically significant differences in antenatal hospital admission rates, operative vaginal delivery, postpartum haemorrhage, or length of hospital stay.

Infant outcomes

The composite outcome of perinatal morbidity used as the main outcome measure in the ACHOIS trial (death, shoulder dystocia, bone fracture, nerve palsy) was significantly reduced for those receiving specific treatment (one trial, 1030 infants; RR 0.32, 95% CI 0.14 to 0.73) (Crowther 2005). For the outcome shoulder dystocia alone, the reduction in its incidence was only marginally significant (two trials, 1098 infants; RR 0.45, 95% CI 0.19 to 1.04).

The difference in the proportion of babies with birthweight greater than 4000 g (one trial, 1030 infants, RR 0.46, 95% CI 0.34 to 0.63) or greater than the 90th centile (three trials, 223 infants, RR 0.55, 95% CI 0.30 to 0.99) was statistically significant. Babies born to women receiving a form of specific treatment for GDM were less likely to weigh more than 4000 g or greater than the 90th birth centile compared to those born to women receiving routine ANC.

Infants were more likely to be admitted to the neonatal care unit if their mothers received specific treatment for GDM in the ACHOIS trial (1224 infants, RR 1.13, 95% CI 1.03 to 1.23) (Crowther 2005). However, when combining this result with the results of two other trials examining the same outcome (Bancroft 2000; Langer 1989), the effect lost statistical significance (three trials, RR 0.57, 95% CI 0.18 to 1.86), $I^2 = 43\%$).

There were no statistically significant differences in gestational age at delivery, incidence of bone fracture in the infant, incidence of nerve palsy in the infant, perinatal death, infant hypoglycaemia, incidence of respiratory distress syndrome or need for ventilation between the two groups.

Comparison two: oral hypoglycaemics versus insulin therapy

Maternal outcomes

There was a significant reduction in caesarean section rates in women receiving oral hypoglycaemics compared to insulin (two trials, 90 women; RR 0.46, 95% CI 0.27 to 0.77).

There were no statistically significant differences detected in the operative vaginal delivery rates, induction of labour and postpartum haemorrhage.

Infant outcomes

There was no statistically significant difference in the proportion of infants with birthweight greater than 4000 g borne to mothers receiving oral hypoglycaemics compared to mother receiving insulin as therapy for GDM (two trials, 93 infants, RR 1.71, 95% CI 0.60 to 4.86). There were also no statistically significant differences in rates of shoulder dystocia, neonatal care admission, respiratory distress syndrome or the need for ventilation.

Infants of mothers treated with insulin were more likely to develop neonatal hypoglycaemia compared to those of mothers treated with oral hypoglycaemics (two trials, 114 infants. RR 7.68, 95% CI 1.47 to 40.22).

Comparison three: acarbose versus insulin therapy

One trial was included under this comparison (Bertini 2005) with 36 women.

Three infant outcomes were considered under this comparison: birthweight greater than the 90th centile and as a continuous variable, gestational age and neonatal hypoglycaemia. None showed statistically significant differences between the two treatment groups.

Other outcomes

Anxiety scores were assessed at six and three months in Crowther 2005. However, the results were not included in the main analysis as the follow-up rates did not meet the review's attrition bias criteria. The results are presented separately in Table 1 and Table 2.

DISCUSSION

Intensive treatment including specific dietary advice and insulin therapy for gestational diabetes was found to reduce the risk of serious perinatal morbidity in the infant using a composite measure of death, shoulder dystocia, nerve palsy and bone fracture. It is associated with less proportion of babies born weighing more than 4000 g or more than the 90th centile. However, it is associated with increases in special care baby unit admissions and in labour induction rates. Caesarean section rates were not significantly reduced when comparing intensive treatment with standard care. However, intensive treatment was associated with a reduction in the risk of developing pre-eclampsia. Caesarean section rates were significantly reduced when comparing oral hypoglycaemics to insulin as a mode of treatment for gestational diabetes mellitus (GDM).

These results are mainly based on the ACHOIS study (Crowther 2005), being the largest trial included, which used a composite outcome of infant death, shoulder dystocia, nerve palsy and bone fracture. This composite outcome is not considered in the other six studies included in this review, which used single end points. It can be criticised on the basis that shoulder dystocia is subjective. Also, there was a lower average gestational age associated with the lower rate of macrosomia. This may have contributed to the outcomes of the ACHOIS study (Crowther 2005). It is difficult to separate elements of the package of care to identify whether the reduced rate of the composite outcome is due to the dietary advice and treatment of raised blood glucose or the intervention which lead to a lower gestational age and reductions in birthweight which reduce the rate of shoulder dystocia.

Macrosomia was reported as an outcome in seven trials, defined as either birthweight over 4000 g or greater than the 90th centile. Babies of mothers receiving specific treatment for GDM were less likely to weigh more than 4000 g. Apart from the increased risk of operative delivery, which is separately assessed in this review, the significance of being born big remains uncertain. This can only be assessed by studies using long-term end points as primary outcomes.

Caesarean section rate was assessed as an outcome in six trials. The reduction in rate was not significant comparing any specific treatment to standard clinical care (risk ratio 0.94, 95% confidence interval 0.63 to 1.38). However, the difference was significant when comparing oral hypoglycaemic drugs to insulin. This result is based

on two trials ([Hague 2003](#); [Moore 2004](#)) with a total sample size of 90 women. The risk of pre-eclampsia was found to be reduced with specific treatment for GDM. This may well be due to better detection of pre-eclampsia associated with the closer monitoring that women with GDM receive.

The review found significantly higher rate of neonatal admission with intensive treatment based on the ACHOIS trial ([Crowther 2005](#)). This may be because when it is known that a woman has gestational diabetes, her baby will be more closely observed. This may lead to an over-diagnosis of hypoglycaemia or a lower threshold for neonatal admission. The important outcome to assess is whether this is associated with an increase in long-term adverse events.

Overall, the results of this review support the need to offer women with a diagnosis of gestational diabetes specific treatment for GDM for better short-term outcomes. However, it is important to note that there is a lack of long-term, follow-up outcomes for both the mother and the baby. The review does not tell us how to screen or who to screen, nor does it provide enough evidence regarding the best mode of treatment for GDM.

AUTHORS' CONCLUSIONS

Implications for practice

When women have a diagnosis of gestational diabetes, they should be considered for specific treatment in addition to routine antenatal care. However, the decision about whether to offer specific dietary advice or more intensive treatment including insulin or oral drugs is not yet clear. The effect of specific treatment on long-term outcomes in the mother and child is also still unclear.

Implications for research

The review highlights starkly the confusion in this area of healthcare. Consistent and universal recommendations for

the diagnosis of gestational diabetes would improve the generalisability of research findings. The fact that one large trial has shown an improvement in a composite outcome for infant morbidity suggests that women should be offered intensive management. However, further large studies comparing different alternative management strategies, considering different ends of the severity spectrum, and using longer-term single outcomes would be required to make this recommendation stronger.

[Note: the 29 citations in the awaiting classification section of the review may alter the conclusions of the review once assessed.]

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For the current update: R Smyth (RS), while working as Editorial Assistant at the Cochrane Pregnancy and Childbirth Group's editorial base in Liverpool, updated the following sections: Abstract, Types of participants, Methods section, Descriptions of Studies, Methodological quality of included studies and Results section. RS assessed all new studies for inclusion, extracted and entered all the data independently.

Trial authors that provided additional unpublished information and data:

Dr Lynda Gillen; Dr Mark Landon; Dr Christian Briery; Dr Carol Homko; Dr Bridget Hsu-Hage; Dr Ann Dornhorst; Dr John Kitzmiller; Prof Caroline Crowther.

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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), a member of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Bancroft 2000

Methods	Randomised controlled pilot study recruiting from 2 centres. Randomisation method: computer-generated codes, telephone randomisation service used. Blinding of intervention: "the diabetologist was aware of the group to which each woman was randomised but the obstetrician was blinded". Blinding of outcome assessment: not stated. No drop-outs but 12 failed to attend follow-up postnatal measurements. Intention-to-treat analysis: not stated (but all women remained in their allocated groups).
Participants	68 women. Inclusion criteria: impaired glucose tolerance (defined following 75 gm OGTT as fasting < 7.0 mmol/L, 2-hours between 7.8 mmol/L and 11.0 mmol/L). Exclusions: none stated. Setting: specialist diabetic/AN clinics.
Interventions	Monitored group were given standard dietary advice, glucose metabolism was monitored by capillary glucose series 5 days a week, HbA1c was measured monthly (insulin was introduced if 5 or more capillary measurements > 7.0 mmol/L in 1 week), serial ultrasound for growth and amniotic fluid, Doppler studies, CTG monitoring. Unmonitored group received dietary advice, HbA1c monthly but no capillary glucose measurements.
Outcomes	Primary outcome measure was admission to special care baby unit. Secondary outcomes: perinatal morbidity (including birth trauma, metabolic disturbance, gestation at delivery, birthweight), measures of maternal inconvenience, number of antenatal clinic visits, mode of delivery, frequency of insulin use.
Notes	2 women in the unmonitored group developed diabetes mellitus, both were diagnosed postnatally and both delivered prematurely.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

Bertini 2005

Methods	Unblinded randomised controlled trial recruited from 1 centre in Brazil.
Participants	70 women. Inclusion criteria: GDM diagnosed as ≥ 110 mg/dl fasting plasma glucose and ≥ 140 mg/dl OGTT after 2 h of 75 g of glucose.
Interventions	3 groups: insulin as conventional therapy, glyburide, and acarbose. All women received diet and exercise programmes.
Outcomes	Gestational age at birth, Apgar scores, birthweight, neonatal hypoglycaemia.
Notes	

Risk of bias

Treatments for gestational diabetes (Review)

Bertini 2005 (Continued)

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Crowther 2005

Methods	<p>Multi centre trial: 18 centres in Australia and UK.</p> <p>Randomisation method: performed centrally with the use of numbers generated by computer with variable block sizes of 6, 8, and 10.</p> <p>Blinding of intervention and outcome assessment: women that were assigned to the intervention group received a slip indicating a diagnosis of glucose intolerance and the plan for intervention, women assigned to routine care received a slip indicating they did not have GD. The full numerical results of the oral glucose-tolerance test were not released to the women or their providers until after birth, before discharge from hospital.</p> <p>Dropouts: no losses to follow up for primary and secondary clinical outcomes for women. No losses to follow up for primary and secondary outcomes for infants.</p> <p>Intention-to-treat analysis was used.</p>
Participants	<p>1000 women.</p> <p>Inclusion criteria: impaired glucose tolerance (defined as having one or more risk factors for GD on selective screening or a positive 50 g oral glucose challenge test (glucose level 1 hour after glucose challenge at least 7.8 mmol per litre [140 mg per decilitre])), and had a 75 g OGTT at 24 to 34 weeks' gestation in which the venous plasma glucose level was less than 7.8 mmol per litre after an overnight fast and was 7.8 to 11.0 mmol per litre (198 mg per decilitre) at 2 hours).</p> <p>Exclusions: women with previously treated GD or active chronic systemic disease (except essential hypertension), more severe impairment or less than 16 or more than 30 weeks' pregnant.</p> <p>Setting: antenatal clinic.</p>
Interventions	<p>Intervention group: care replicated clinical care in which universal screening and treatment for GD was available, individualised dietary advice from a qualified dietician, instructions on how to self-monitor glucose levels 4 times a day until fasting glucose levels of at least 3.5 mmol per litre [63 mg per decilitre] and no more than 5.5 mmol per litre [99 mg per decilitre], preprandial levels of no more than 5.5 mmol per litre, and levels 2 hours postprandially that were no more than 7.0 mmol per litre [126 mg per decilitre], followed by daily monitoring at rotating times during the day; and insulin therapy, with the dose adjusted based on glucose levels, if there were 2 capillary-blood glucose results during the 2-week period in which the fasting level was at least 5.5 mmol per litre or the postprandial level was at least 7.0 mmol per litre at 35 weeks' gestation or less, if the postprandial level was at least 8.0 mmol per litre (144 mg per decilitre) at more than 35 weeks' gestation, or if one capillary-blood glucose results during the 2-week period was at least 9.0 mmol per litre (162 mg per decilitre).</p> <p>Control group: care replicated clinical care in which screening for GD was not available, women and caregivers were not aware of the diagnosis of glucose intolerance, at the discretion of the attending clinician, if indications arose that were suggestive of diabetes, further assessment for GD was permitted, with treatment as considered appropriate.</p>
Outcomes	<p>Primary outcomes - infant: composite measures of serious perinatal complications (defined as 1 or more of death, shoulder dystocia, bone fracture, and nerve palsy), admission to neonatal nursery, and jaundice requiring phototherapy.</p> <p>Primary outcomes - women: need for IOL and caesarean section, health status, and psychological outcomes.</p> <p>Secondary outcomes - infant: gestational age at birth, birthweight, Apgar score of less than 7 at 5 minutes, hypoglycaemia requiring IV therapy, convulsions, RDS.</p> <p>Secondary outcomes - women: number of prenatal visits to a health professional, mode of birth, weight during pregnancy, number of antenatal admissions, presence or absence of PIH, perineal trauma, PPH, breastfeeding at hospital discharge.</p>

Crowther 2005 (Continued)

Notes	93% of the women had been found to be at risk of GD on the basis of OGTT, and the remainder on the basis of risk factors. 5 perinatal deaths (3 stillbirths and 2 neonatal deaths) occurred in the control group: 2 stillbirths were unexplained intrauterine deaths at term of appropriately grown infants, and 1 at 35 weeks' gestation, was associated with pre-eclampsia and intrauterine growth restriction. 1 infant had a lethal congenital anomaly, and 1 infant died after an asphyxial condition during labour with antepartum haemorrhage. After consent had been obtained, a proportion of the women (not fewer than 1 in 5) who had normal oral GTT results were assigned to the routine-care group to help maintain blinding.
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Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

Ford 1997

Methods	Single centre randomised trial. Randomisation method: sealed opaque envelopes. Blinding of intervention: not stated. Blinding of outcome assessment: not stated. Dropouts: 5 withdrawn from the study - 3 for insulin therapy, other 2 unaccounted for (possibly withdrawn following dietary advice but unclear). Intention-to-treat analysis: not stated.
Participants	29 women. Inclusion criteria: impaired glucose tolerance (defined following a 75 g OGTT as 2-hour plasma glucose level between 8 mmol/L and 11 mmol/L). Exclusions: none stated. Setting: joint diabetic/AN clinic.
Interventions	Dietary treatment group were given specific 'diabetic type' advice (i.e. 'high fibre, high carbohydrate, low fat and appropriate energy'). The control group received no specific dietary advice. Both groups attended clinic weekly and performed plasma glucose profiles.
Outcomes	Outcomes measured: caesarean section, birthweight, use of insulin.
Notes	If plasma glucose levels were raised in the non-diet group they were given dietary advice or insulin therapy, or both. An attempt to diagnose macrosomia by ultrasound was made from 30 weeks in both groups. The trial did not recruit its expected sample.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Gillen 2004

Methods	Single centre randomised controlled trial.
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Gillen 2004 (Continued)

Randomisation method: open table of random numbers constructed by an independent person and kept confidential from members of the study team. Women were matched consecutively to the next available number in the table and the study team informed of the result.
Blinding of intervention: yes, participants unaware of differences in advice between intervention and control groups.
Blinding of outcome assessment: not stated.
Intention-to-treat analysis was used.
Dropouts: data not available for 1 woman from each group.

Participants	32 women. Inclusion criteria: GDM (defined on an OGTT defined by the Australian Diabetes in Pregnancy Society). Exclusions: significant other health concerns, poor English language skills. Setting: diabetic clinic. Intention-to-treat analysis was used.	
Interventions	Control group: standard clinical practice (individualised carbohydrate portion-controlled meal plan, with low-fat and low-glycaemic index dietary strategies and general advice about meeting nutritional requirements of pregnancy). Intervention group: standard clinical practice as above, plus advice for targeted intakes of foods rich in unsaturated fats.	
Outcomes	Outcomes: gestation at delivery, mode of delivery.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

Hague 2003

Methods	Pilot study in Australia. Randomisation method: 'women randomised'. Blinding of intervention: not stated. Blinding of outcome assessment: not stated. Dropouts: none reported. Intention-to-treat analysis: not stated.
Participants	30 women. Inclusion criteria: GD diagnosed by the criteria of the Australasian Diabetes in Pregnancy Society. Exclusions: not stated. Setting: not stated.
Interventions	Intervention group: metformin. Control group: insulin.
Outcomes	Outcomes: mode of delivery, pre-eclampsia, fetal beta cell activity, birthweight, median time in SCBU, neonatal jaundice, need for neonatal phototherapy.
Notes	
Risk of bias	

Hague 2003 (Continued)

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Langer 1989

Methods	Described as a "randomised trial" - no further information. Method of randomisation: computer-generated list (information obtained directly from the author). Blinding of intervention: not stated. Blinding of outcome assessment: not stated. Participation rates not given, no dropouts/withdrawals reported. Intention-to-treat analysis: not stated.	
Participants	126 women (a further 146 with normal OGTT results were used as a control group but their data have not been included in this review). Inclusion criteria: 1 abnormal value following 100 g OGTT (according to National Diabetes Data Group values fasting > 105 mg/dl, 1-hour > 10.6 mg/dl, 2-hour > 165 mg/dl, 3-hour > 145 mg/dl). Exclusions: none stated. Setting: medical centre.	
Interventions	3 groups in this study - 'treated', 'untreated' and a control group of women with normal screening/OGTT results. (Data for this group are not included in this review.) All participants monitored capillary blood glucose 7 times/day. (This was just for a 4-week period for the untreated group.) Treated group were managed according to diabetic protocol including dietary advice (determined by pre-pregnancy body mass index), insulin treatment based on 0.7 units per kg of body weight measured in pregnancy. The untreated group continued normal eating patterns.	
Outcomes	Outcomes measured: gestation at delivery, weight gain, caesarean section, hypertensive disorder, birthweight, prematurity, neonatal hypoglycaemia, neonatal hyperbilirubinemia, neonatal polycythemia, NICU admission.	
Notes	National diabetes data group criteria include 4 values: fasting, 1-hour, 2-hour, 3-hour.	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Moore 2004

Methods	Single centre randomised trial. Randomisation method: list of tables used, sealed envelopes. Blinding of intervention: not stated. Blinding of outcome assessment: no. Dropouts: none.	
Participants	63 women. Inclusion criteria: impaired glucose tolerance (based on 100 g oral OGTT). Exclusions: insulin-dependent diabetes mellitus, liver/kidney disease, chronic hypertension or seizure disorders, less than 11 weeks or more than 36 weeks' gestation.	

Moore 2004 (Continued)

Setting: not stated.

Interventions	Intervention group: insulin. Control group: metformin.
Outcomes	Gestational age at birth, mode of delivery, shoulder dystocia, PPH, birthweight, Apgar score at 5 minutes, NICU admission, hypoglycaemia, RDS, hyperbilirubinemia.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

AN: antenatal
 CTG: cardiotocography
 GD: gestational diabetes
 GDM: gestational diabetes mellitus
 GTT: glucose tolerance test
 h: hour
 IOL: induction of labour
 IV: intravenous
 NICU: neonatal intensive care unit
 OGTT: oral glucose tolerance test
 PIH: pregnancy-induced hypertension (defined as blood pressure of at least 140/90)
 PPH: postpartum haemorrhage
 RDS: respiratory distress syndrome
 SCBU: special care baby unit

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Anjalakshi 200	Not correct outcomes for this review.
Bevier 1999	Not predetermined population; those studied had normal OGTT results.
Bonomo 2004	Not correct population for this review.
Bonomo 2005	Used 50 g glucose challenge test. Not correct population for this review.
Brankston 2004	Not correct intervention for this review - comparing exercise.
Buchanan 1994	Not correct population for this review. Population studied were those with a fetal abdominal circumference above 75th centile.
Bung 1991	Not correct diagnostic criteria for this review. Eligibility was based on persistent fasting plasma glucose at values not matching those specified for this review (5.8 mM-7.22 mM).
Coustan 1978	Not truly randomised. First 20 women were assigned treatment based on gestation.
Cypryk 2007	Outcomes measures used not under outcomes considered by this review.

Treatments for gestational diabetes (Review)

Study	Reason for exclusion
De Veciana 2002	Not predetermined population or intervention for this review.
Di Cianni 2007	Compares two types of insulin (short acting versus regular insulin).
Dornhorst 1989	No data available.
Dunne 2001	No published or unpublished information on this trial, unable to trace author.
Garner 1997	Not diagnostic criteria specified for this review. This study used 2-hour upper limits of 7.5 mmol/l for women in 2nd trimester and 9.6 mmol/l for women in 3rd trimester.
Gillmer 1986	Diagnosis by 50 g OGTT. Not randomised.
Graham 2005	Not predetermined intervention for this review (Cinnamon).
Homko 2002	Eligibility criteria: all women underwent a 3-hour OGTT and needed to have 2 abnormal values based on the Carpenter-Coustan criteria but a normal FBS (< 95 mg/dl).
Hopp 1996	Diagnosis by 50 g OGTT.
Ilic 1999	Outcomes measures used not under outcomes considered by this review.
Jovanovic 1999	Not correct intervention for this review - comparing regular human insulin with insulin lispro.
Jovanovic-Peterson 1989	Not truly randomised, inadequate baseline comparability of groups.
Jovanovic-Peterson 1993	Not an intervention predetermined by this review.
Kitzmiller 1990	Informed by author that trial never started (March 2006).
Kjos 2001	Inclusion based on 1 fasting glucose result. Therefore not the correct inclusion criteria for this review.
Langer 1994	Not randomised.
Langer 2000	Eligibility criteria: fasting glucose of more than 5.3.
Lao 2001	Correspondence, not a study.
Lauszus 2001	Not the correct outcomes for this review.
Lesser 1996	Crossover design.
Li 1987	Not true randomisation.
Li 1999	Not randomised - allocation by consent to treatment.
Magee 1990	Not predetermined outcomes and specific to obese women.
Mecacci 2003	Not correct intervention for this review - comparing 2 types of insulin.
MRC 1955	Not correct population for this review.
Nolan 1984	Crossover design, no control group.

Study	Reason for exclusion
Nor Azlin 2007	Not correct intervention for this review. Comparing 2 types of insulin (short vs intermediate acting). No diagnostic criteria specified.
Notelovitz 1971	Population includes established diabetics - impossible to distinguish between established and gestational in the data.
O'Sullivan 1971	Not randomised, alternate allocation.
O'Sullivan 1974	Primary outcome death. No details of randomisation, no intention-to-treat analysis. Endpoints unclear.
O'Sullivan 1980	Not randomised.
Pardi 1989	Study not completed, insufficient data collected to analyse.
Persson 1985	Raw data no longer available for analysis.
Pettitt 2003	Not correct outcomes measures.
Pettitt 2007	Not correct intervention for this review - comparing 2 types of insulin. Not correct diagnostic criteria.
Polyhonen-Alho 2002	Not correct diagnostic criteria for this review. Diagnosis of GD was made on the following values: fasting 4.8 mmol/l, 2-hour 8.7 mmol/l.
Rae 2000	Incorrect population for this review - obese women only.
Reader 2006	Cluster RCT. Diagnostic criteria not specified.
Reece 1995	Diagnosis of gestational diabetes not clearly defined. HbA1c levels only given for IDDM.
Rey 1995	Review criteria not met. This was a study of a sweet breakfast screening test therefore, not the appropriate diagnostic criteria for this review.
Rey 1997	Not correct diagnostic criteria for this review. Some participants were included in the study following 50 g glucose screen. OGTT diagnostic values used did not match the criteria for this review.
Rossi 2000	Not correct diagnostic criteria for this review. This study diagnosed GD by the following values: fasting 95 mg/dl, 1-hour 180 mg/dl, 2-hour 155 mg/dl, 3-hour 140 mg/dl.
Schaefer-Graf 2004	Not correct population for this review.
Schuster 1998	Incorrect population.
Silva 2005	Not predetermined diagnostic criteria of GDM.
Snyder 1998	Eligibility was by OGTT results or 50 g screening test - 50 g screening test not correct eligibility criteria for this review.
Thompson 1990	Gestational diabetes and IGT not divided. Unable to separate data.
Todorova 2007	Economic analysis.
Yang 2003	Attrition rate of 50%.

FBS: fasting blood sugar
GD: gestational diabetes
IDDM: insulin-dependent diabetes mellitus
IGT: impaired glucose tolerance
OGTT: oral glucose tolerance test
RCT: randomised controlled trial
vs: versus

Characteristics of ongoing studies [ordered by study ID]

Crowther 2007

Trial name or title	Dietary and lifestyle advice for women with borderline gestational glucose intolerance.
Methods	
Participants	All pregnant women between 24 weeks and 0 day and 29 weeks and 6 days gestation with a singleton pregnancy, attending antenatal clinics at the collaborating hospitals, with a positive OGCT (plasma glucose greater than or equal to 7.8mmol/L) and a normal OGTT (fasting venous plasma glucose less than 5.5 mmol/L and a 2-hour glucose less than 7.8 mmol/L), who give written, informed consent. There is no age limit criteria for this trial. There is no minimum age limit for the mother.
Interventions	Individualised advice regarding their diet from a qualified dietician, based on published recommendations of the Dieticians Association of Australia, that are culturally appropriate and meet the nutritional requirements of pregnancy. Moderate exercise is recognised as an adjunct to dietary advice compared with routine pregnancy care.
Outcomes	1. Risk of infant morbidity (measured by serious perinatal complications, number of large for gestational age infants, neonatal jaundice requiring phototherapy and neonatal hypoglycaemia requiring treatment); measured once, at time of primary hospital discharge or death prior to discharge. 2. Risk of maternal physical morbidity (measured by need for induction of labour, need for caesarean section and pre-eclampsia); measured up to primary hospital discharge. 3. Maternal psychological outcomes and health status (as measured by anxiety, depression and health related quality of life).
Starting date	Not yet recruiting.
Contact information	caroline.crowther@adelaide.edu.au
Notes	

Golladay 2006

Trial name or title	Randomised trial of treatment for gestational diabetes.
Methods	
Participants	Pregnant women over age 18 who fail to achieve adequate glucose control on diet therapy alone.
Interventions	Glyburide.
Outcomes	Primary outcome measure: newborn birthweight. Secondary outcome measures: gestational age at delivery;

Golladay 2006 (Continued)

	method of delivery (caesarean, forceps, vacuum, spontaneous); complications of delivery (shoulder dystocia, birth injury, 4th degree vaginal laceration); newborn intensive care unit admission; congenital anomalies of the newborn; incidence of neonatal metabolic derangement.
Starting date	June 2004.
Contact information	Elizabeth C Golladay elizabeth.golladay@us.army.mil
Notes	

Kipikasa 2008

Trial name or title	Comparison of Glucovance to Insulin for Diabetes During Pregnancy.
Methods	
Participants	24-28 weeks' gestations with diagnostic OGTT.
Interventions	Glucovance (glyburide and metformin) versus insulin therapy.
Outcomes	Primary outcome measures: maternal hemoglobin A1C at delivery; maternal fructosamine at delivery; maternal glucose at delivery. Secondary outcome measures: mode of delivery; infant birthweight; infant initial glucose; infant complications.
Starting date	Recruiting.
Contact information	Joseph H Kipikasa, MD Regional Obstetrical Consultants; UT Chattanooga OB-GYN Department.
Notes	Estimated completion date September 2008.

Landon 2002

Trial name or title	A randomised clinical trial of treatment for mild gestational diabetes mellitus.
Methods	
Participants	Pregnant women, with singleton pregnancies, diagnosed with mild gestational diabetes (1-hour glucose loading test result between 135 and 200 mg/dl followed by a 3-hour OGTT with normal fasting, ie less than 95 mg/dl) between 24 and 29 weeks' gestation.
Interventions	Diet therapy and insulin as required versus no specific treatment.
Outcomes	Composite outcome of neonatal morbidity.

Treatments for gestational diabetes (Review)

Landon 2002 (Continued)

Starting date	We do not have this information.
Contact information	Dr Mark B Landon. Email address mlandon@columbus.rr.com
Notes	07/03/06 - Information from trialist: the trial is ongoing for approximately 18 additional months.

Rowan 2005

Trial name or title	The Metformin in Gestational Diabetes (MiG) Trial.
Methods	
Participants	Women aged 18-45 with singleton pregnancies with fasting glucose > 5.4 or 2 hour GTT > 6.7 mmol/l.
Interventions	Metformin versus insulin therapy.
Outcomes	Perinatal complications, neonatal anthropometry.
Starting date	We do not have this information.
Contact information	Janet A Rowan. Email jrowan@internet.co.nz
Notes	

GTT: glucose tolerance test

OGCT: oral glucose challenge test

OGTT: oral glucose tolerance test

DATA AND ANALYSES

Comparison 1. Any specific treatment versus routine antenatal care (subgroups by type of specific treatment)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Antenatal hospital visits	1	68	Mean Difference (IV, Fixed, 95% CI)	1.0 [-1.63, 3.63]
1.1 Specific dietary advice	1	68	Mean Difference (IV, Fixed, 95% CI)	1.0 [-1.63, 3.63]
2 Antenatal hospital admissions	1	1000	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.87, 1.29]
2.1 Package of treatment for mild GDM	1	1000	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.87, 1.29]
3 Number of extra blood tests	1	28	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.1 Specific dietary advice	1	28	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Treatments for gestational diabetes (Review)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Pre-eclampsia	1	1000	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.48, 0.88]
4.1 Package of treatment for mild GDM	1	1000	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.48, 0.88]
5 Need for insulin treatment	3	1097	Risk Ratio (M-H, Fixed, 95% CI)	5.68 [3.56, 9.04]
5.1 Package of treatment for mild GDM	1	1000	Risk Ratio (M-H, Fixed, 95% CI)	6.12 [3.72, 10.08]
5.2 Specific dietary advice	2	97	Risk Ratio (M-H, Fixed, 95% CI)	2.90 [0.77, 10.89]
6 Induction of labour	2	1068	Risk Ratio (M-H, Fixed, 95% CI)	1.33 [1.13, 1.57]
6.1 Package of treatment for mild GDM	1	1000	Risk Ratio (M-H, Fixed, 95% CI)	1.31 [1.10, 1.56]
6.2 Specific dietary advice	1	68	Risk Ratio (M-H, Fixed, 95% CI)	1.5 [0.94, 2.40]
7 Operative vaginal delivery	1	68	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.07, 17.26]
7.1 Specific dietary advice	1	68	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.07, 17.26]
8 Caesarean section	5	1255	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.80, 1.12]
8.1 Package of treatment for mild GDM	1	1000	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.80, 1.16]
8.2 Specific dietary advice	3	129	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.45, 1.62]
8.3 Diet plus insulin for mixed severity	1	126	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.36, 1.84]
9 Postpartum haemorrhage	1	1000	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.58, 1.54]
9.1 Package of treatment for mild GDM	1	1000	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.58, 1.54]
10 Gestational age at delivery	3	226	Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.43, 0.32]
10.1 Specific dietary advice	2	100	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.61, 0.41]
10.2 Diet plus insulin for mixed severity	1	126	Mean Difference (IV, Fixed, 95% CI)	0.0 [-0.55, 0.55]
11 Birthweight > 4000 g	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.34, 0.63]
11.1 Package of treatment for mild GDM	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.34, 0.63]
12 Birthweight > 90th centile	3	223	Risk Ratio (M-H, Fixed, 95% CI)	0.55 [0.30, 0.99]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.1 Specific dietary advice	2	97	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.44, 1.97]
12.2 Diet plus insulin for mixed severity	1	126	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.09, 0.76]
13 Perinatal death	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.09 [0.01, 1.70]
13.1 Package of treatment for mild GDM	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.09 [0.01, 1.70]
14 Bone fracture in infant	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.35 [0.01, 8.45]
14.1 Package of treatment for mild GDM	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.35 [0.01, 8.45]
15 Nerve palsy in infant	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.15 [0.01, 2.86]
15.1 Package of treatment for mild GDM	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.15 [0.01, 2.86]
16 Shoulder dystocia	2	1098	Risk Ratio (M-H, Fixed, 95% CI)	0.45 [0.19, 1.04]
16.1 Package of treatment for mild GDM	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.45 [0.19, 1.09]
16.2 Specific dietary advice	1	68	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.02, 8.86]
17 Composite outcome in infant (death, shoulder dystocia, nerve palsy, bone fracture)	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.14, 0.73]
17.1 Package of treatment for mild GDM	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.14, 0.73]
18 Admission to neonatal care/special baby care unit	3	1224	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [1.03, 1.23]
18.1 Package of treatment for mild GDM	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [1.05, 1.26]
18.2 Specific dietary advice	1	68	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.08, 1.73]
18.3 Diet plus insulin for mixed severity	1	126	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.18, 1.86]
19 Respiratory distress syndrome/need for ventilation in infant	2	1098	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [0.86, 2.63]
19.1 Package of treatment for mild GDM	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	1.47 [0.83, 2.61]
19.2 Specific dietary advice	1	68	Risk Ratio (M-H, Fixed, 95% CI)	2.25 [0.21, 23.66]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
20 Neonatal hypoglycemia	3	1224	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.63, 1.48]
20.1 Package of treatment for mild GDM	1	1030	Risk Ratio (M-H, Fixed, 95% CI)	1.34 [0.82, 2.18]
20.2 Specific dietary advice	1	68	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.08, 1.73]
20.3 Diet plus insulin for mixed severity	1	126	Risk Ratio (M-H, Fixed, 95% CI)	0.13 [0.02, 0.97]
21 Length of hospital stay (days)	1	66	Mean Difference (IV, Fixed, 95% CI)	0.97 [-0.46, 2.40]
21.1 Specific dietary advice	1	66	Mean Difference (IV, Fixed, 95% CI)	0.97 [-0.46, 2.40]

Analysis 1.1. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 1 Antenatal hospital visits.

Study or subgroup	Specific treatment		Routine ANC		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
1.1.1 Specific dietary advice							
Bancroft 2000	32	15.5 (6)	36	14.5 (4.9)		100%	1[-1.63,3.63]
Subtotal ***	32		36			100%	1[-1.63,3.63]
Heterogeneity: Not applicable							
Test for overall effect: Z=0.75(P=0.46)							
Total ***	32		36			100%	1[-1.63,3.63]
Heterogeneity: Not applicable							
Test for overall effect: Z=0.75(P=0.46)							
					Favours experimental	-100 -50 0 50 100	Favours control

Analysis 1.2. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 2 Antenatal hospital admissions.

Study or subgroup	Specific treatment	Routine ANC	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
	n/N	n/N			
1.2.1 Package of treatment for mild GDM					
Crowther 2005	141/490	139/510		100%	1.06[0.87,1.29]
Subtotal (95% CI)	490	510		100%	1.06[0.87,1.29]
Total events: 141 (Specific treatment), 139 (Routine ANC)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.54(P=0.59)					
Total (95% CI)	490	510		100%	1.06[0.87,1.29]
Total events: 141 (Specific treatment), 139 (Routine ANC)					
			Favours experimental	0.01 0.1 1 10 100	Favours control

Analysis 1.3. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 3 Number of extra blood tests.

Analysis 1.4. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 4 Pre-eclampsia.

Analysis 1.5. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 5 Need for insulin treatment.

Analysis 1.6. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 6 Induction of labour.

Study or subgroup	Specific treatment n/N	Routine ANC n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Test for subgroup differences: $\chi^2=0.28$, $df=1$ ($P=0.6$), $I^2=0\%$					
Favours experimental 0.01 0.1 1 10 100 Favours control					

Analysis 1.7. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 7 Operative vaginal delivery.

Study or subgroup	Specific treatment n/N	Routine ANC n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.1 Specific dietary advice					
Bancroft 2000	1/32	1/36		100%	1.13[0.07,17.26]
Subtotal (95% CI)	32	36		100%	1.13[0.07,17.26]
Total events: 1 (Specific treatment), 1 (Routine ANC)					
Heterogeneity: Not applicable					
Test for overall effect: $Z=0.08$ ($P=0.93$)					
Total (95% CI)	32	36		100%	1.13[0.07,17.26]
Total events: 1 (Specific treatment), 1 (Routine ANC)					
Heterogeneity: Not applicable					
Test for overall effect: $Z=0.08$ ($P=0.93$)					
Favours experimental 0.01 0.1 1 10 100 Favours control					

Analysis 1.8. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 8 Caesarean section.

Study or subgroup	Specific treatment n/N	Routine ANC n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.8.1 Package of treatment for mild GDM					
Crowther 2005	152/490	164/510		86.23%	0.96[0.8,1.16]
Subtotal (95% CI)	490	510		86.23%	0.96[0.8,1.16]
Total events: 152 (Specific treatment), 164 (Routine ANC)					
Heterogeneity: $\tau^2=0$; $\chi^2=0$, $df=0$ ($P<0.0001$); $I^2=100\%$					
Test for overall effect: $Z=0.39$ ($P=0.7$)					
1.8.2 Specific dietary advice					
Bancroft 2000	10/32	11/36		5.55%	1.02[0.5,2.08]
Ford 1997	1/16	3/13		1.78%	0.27[0.03,2.31]
Gillen 2004	1/16	1/16		0.54%	1[0.07,14.64]
Subtotal (95% CI)	64	65		7.87%	0.85[0.45,1.62]
Total events: 12 (Specific treatment), 15 (Routine ANC)					
Heterogeneity: $\tau^2=0$; $\chi^2=1.37$, $df=2$ ($P=0.5$); $I^2=0\%$					
Test for overall effect: $Z=0.49$ ($P=0.63$)					
1.8.3 Diet plus insulin for mixed severity					
Langer 1989	9/63	11/63		5.9%	0.82[0.36,1.84]
Favours experimental 0.01 0.1 1 10 100 Favours control

Analysis 1.9. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 9 Postpartum haemorrhage.

Analysis 1.10. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 10 Gestational age at delivery.

Analysis 1.11. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 11 Birthweight > 4000 g.

Analysis 1.12. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 12 Birthweight > 90th centile.

Analysis 1.13. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 13 Perinatal death.

Analysis 1.14. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 14 Bone fracture in infant.

Analysis 1.15. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 15 Nerve palsy in infant.

Analysis 1.16. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 16 Shoulder dystocia.

Analysis 1.17. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 17 Composite outcome in infant (death, shoulder dystocia, nerve palsy, bone fracture).

Analysis 1.18. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 18 Admission to neonatal care/special baby care unit.

Analysis 1.19. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 19 Respiratory distress syndrome/need for ventilation in infant.

Analysis 1.20. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 20 Neonatal hypoglycemia.

Analysis 1.21. Comparison 1 Any specific treatment versus routine antenatal care (subgroups by type of specific treatment), Outcome 21 Length of hospital stay (days).

Comparison 2. Oral hypoglycemic drugs versus insulin therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caesarean section	2	90	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.27, 0.77]
2 Operative vaginal delivery	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.02, 8.59]
3 Induction of labour	1	30	Risk Ratio (M-H, Fixed, 95% CI)	2.06 [0.90, 4.69]
4 Postpartum haemorrhage	1	63	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.01, 8.13]
5 Gestational age at delivery	3	144	Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.52, 0.42]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Birthweight > 4000 g	2	93	Risk Ratio (M-H, Fixed, 95% CI)	1.71 [0.60, 4.86]
7 Birthweight > 90th centile	1	51	Risk Ratio (M-H, Fixed, 95% CI)	6.75 [0.87, 52.14]
8 Birthweight (g)	1	51	Mean Difference (IV, Fixed, 95% CI)	244.40 [-15.61, 504.41]
9 Neonatal hypoglycemia	2	114	Risk Ratio (M-H, Fixed, 95% CI)	7.68 [1.47, 40.22]
10 Admission to neonatal care/special baby care unit	1	63	Risk Ratio (M-H, Fixed, 95% CI)	2.06 [0.41, 10.47]
11 Shoulder dystocia	1	63	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.01, 8.13]
12 Respiratory distress syndrome/need for ventilation in infant	1	63	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.10, 2.62]

Analysis 2.1. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 1 Caesarean section.

Analysis 2.2. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 2 Operative vaginal delivery.

Analysis 2.3. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 3 Induction of labour.

Analysis 2.4. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 4 Postpartum haemorrhage.

Analysis 2.5. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 5 Gestational age at delivery.

Analysis 2.6. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 6 Birthweight > 4000 g.

Analysis 2.7. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 7 Birthweight > 90th centile.

Analysis 2.8. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 8 Birthweight (g).

Analysis 2.9. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 9 Neonatal hypoglycemia.

Analysis 2.10. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 10 Admission to neonatal care/special baby care unit.

Analysis 2.11. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 11 Shoulder dystocia.

Analysis 2.12. Comparison 2 Oral hypoglycemic drugs versus insulin therapy, Outcome 12 Respiratory distress syndrome/need for ventilation in infant.

Comparison 3. Acarbose versus insulin therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Gestational age at delivery	1	46	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-1.00, 0.40]
2 Birthweight (g)	1	46	Mean Difference (IV, Fixed, 95% CI)	91.40 [-145.32, 328.12]
3 Birthweight > 90th centile	1	46	Risk Ratio (M-H, Fixed, 95% CI)	2.84 [0.28, 29.14]
4 Neonatal hypoglycemia	1	46	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.09, 21.34]

Analysis 3.1. Comparison 3 Acarbose versus insulin therapy, Outcome 1 Gestational age at delivery.

Analysis 3.2. Comparison 3 Acarbose versus insulin therapy, Outcome 2 Birthweight (g).

Analysis 3.3. Comparison 3 Acarbose versus insulin therapy, Outcome 3 Birthweight > 90th centile.

Analysis 3.4. Comparison 3 Acarbose versus insulin therapy, Outcome 4 Neonatal hypoglycemia. **ADDITIONAL TABLES****Table 1. Anxiety score 6 weeks after enrolment**

treatment (N)	treatment (mean)	treatment (SD)	control (N)	control (mean)	control (SD)
332	11.20	3.70	350	11.50	4.00

Table 2. Anxiety score 3 months after enrolment

treatment (N)	treatment (mean)	treatment (SD)	control (N)	control (mean)	control (SD)
278	10.60	3.90	295	10.80	3.80

APPENDICES**Appendix 1. CENTRAL search strategy used in previous version of the review**

#1 pregnan*
#2 pregnancy (MeSH - explode all trees)
#3 pregnancy complications (MeSH - explode all trees)
#4 antepart*
#5 antenatal
#6 perinatal
#7 postnatal
#8 postpart*
#9 obstetric*
#10 gestation*
#11 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
#12 diabet*
#13 diabetes mellitus (MeSH - explode all trees)
#14 macrosomi*
#15 #12 OR #13 OR #14
#16 #15 AND #11

WHAT'S NEW

Date	Event	Description
1 July 2011	Amended	Search updated. Nineteen trial reports added to Studies awaiting classification .

HISTORY

Protocol first published: Issue 4, 2001

Review first published: Issue 3, 2003

Date	Event	Description
31 January 2009	New search has been performed	Search updated in April 2008. Five new trials included: Bertini 2005 ; Crowther 2005 ; Gillen 2004 ; Hague 2003 ; Moore 2004 . The results of the January 2009 search have been added to the Studies awaiting classification section.
12 November 2008	Amended	Converted to new review format.
31 January 2008	New citation required and conclusions have changed	There is now evidence that offering specific treatment for gestational diabetes may be associated with better baby and mother outcomes, but has not found robust evidence on the best choice of treatment which provides the better outcome for these women and their babies.

CONTRIBUTIONS OF AUTHORS

D Tuffnell (DT), J West (JW), S Walkinshaw (SW) were involved in the planning and approval of the first version of the review. DT and JW wrote the protocol and text of the review incorporating comments from SW. The review was updated by N Alwan, DT and JW with the support of the Cochrane Pregnancy and Childbirth Group editorial base (see '[Acknowledgements](#)').

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- The University of Liverpool, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We added the outcome 'composite' (defined as one or more of the following: infant death, shoulder dystocia, bone fracture and nerve palsy) to the list of neonatal outcomes. Although this outcome was not included in the original protocol for the review, it has been added as it is the primary outcome used by the ACHOIS trial ([Crowther 2005](#)), which includes the biggest sample among all the other studies included in this review.

NOTES

This updated review was prepared before the release of RevMan 5 and the new Risk of bias tables. This update was therefore prepared in an earlier version of RevMan and converted to RevMan 5 during the editorial processing of the updated review. The Risk of bias tables have therefore not been completed for this updated review and it does not draw on the Group's updated methodology, as described within the editorial information about the [Cochrane Pregnancy and Childbirth Group](#), which were developed to reflect the new statistical options available in RevMan 5. For future updates, the new risk of bias assessments will be described for new studies (identified through updated searches) that meet the inclusion criteria.

INDEX TERMS

Medical Subject Headings (MeSH)

Blood Glucose [metabolism]; Diabetes, Gestational [blood] [*therapy]; Glucose Tolerance Test; Pregnancy Outcome; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Pregnancy