### Topic proposal

I understand that this proposal will be retained by the SIGN Programme Lead and be made available on the SIGN website for time period that the proposal is being considered. **Only proposals with a completed Declaration of Interests for the principal proposer will be considered.**

<table>
<thead>
<tr>
<th>1. What is the problem/need for a guideline/clinical scenario?</th>
</tr>
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<tbody>
<tr>
<td>The existing guideline on management of diabetes in pregnancy and screening and management of gestational diabetes, published as a chapter in the 2010 general SIGN guideline on diabetes (SIGN 116) is becoming out of date. We understand that the complete SIGN guideline may not be updated and would suggest that a standalone guideline for diabetes in pregnancy would be preferable.</td>
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<table>
<thead>
<tr>
<th>2. Burden of the condition</th>
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<tbody>
<tr>
<td>Mortality of women with pre-existing diabetes in pregnancy is increased but is thankfully very rare so the absolute burden is small. Morbidity is considerable with a 4-5 fold increase in stillbirth and perinatal mortality in women with type 1 and type 2 diabetes, increased risk of preeclampsia, pre-term birth and operative delivery. There is also considerable burden associated with management of the condition with requirement for very frequent blood glucose monitoring and intensive insulin management.</td>
</tr>
<tr>
<td>Incidence: Depending on screening pathways 4-10% of pregnancies are complicated by incident gestational diabetes.</td>
</tr>
<tr>
<td>Prevalence: We have excellent national figures - around 1 in 200 pregnancies is complicated by pre-existing diabetes (70% type 1 diabetes and 30% type 2 diabetes).</td>
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<tr>
<th>3. Variations</th>
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<tbody>
<tr>
<td>In practice in Scotland: following the SIGN guideline there would appear to be relatively homogeneous provision of joint multidisciplinary clinics (diabetes, obstetric, midwifery). We have identified very major differences in screening pathways for gestational diabetes between and sometimes within health boards. This predominantly relates to which risk factors for GDM prompt screening. Obesity is a major risk factor but it is clear from a recent survey of clinicians involved in Scotland that the threshold for screening varies from 30kg/m$^2$ to 40kg/m$^2$ in different areas. This would appear indefensible and has arisen due to different resource allocation to screening in different areas.</td>
</tr>
<tr>
<td>In health outcomes in Scotland: National datasets address outcomes for women with T1DM and T2DM- while worse than the background population these would appear similar between health boards. No equivalent data exist for outcomes for GDM- but given the great variation in screening it would appear likely that these are much more heterogeneous.</td>
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<tr>
<th>4. Areas of uncertainty to be covered</th>
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<tbody>
<tr>
<td><strong>Key question 1:</strong> Application of novel glucose sensing technologies to management of women with diabetes in pregnancy. There have been major advances in glucose monitoring technologies in the last 5 years. In the case of continuous glucose monitoring this has been assessed in an RCT published in the Lancet in 2017. This requires update. We note that NICE recently announced that they would carry out a limited review of these technologies. We await the timeline of this and it may well be that either conclusions or evidence tables of this review could be used or incorporated.</td>
</tr>
<tr>
<td><strong>Key question 2:</strong> Screening pathways for gestational diabetes require revision in two main areas. The following questions were developed at a consensus meeting of the Scottish Diabetes Group Diabetes and Pregnancy subgroup:</td>
</tr>
<tr>
<td>1) Second trimester screening is carried out at 24-28 weeks. The previous SIGN guideline endorsed the diagnostic criteria of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) subsequently adopted by the World Health Organisation(WHO). By contrast NICE have adopted a different set of criteria although...</td>
</tr>
</tbody>
</table>
we understand that these are not fully adopted in all areas of England and Wales.

a) What is the evidence for WHO/IADPSG vs NICE criteria?
b) Is screening low risk women with random or fasting glucose clinically effective?

2) Testing for pre-existing (but undiagnosed) diabetes in early pregnancy appears increasingly important as the metabolic health of the pregnant population declines due to age and obesity. The best screening approach to this and early detection of gestational diabetes is unclear and not well covered in current guidelines (SIGN or NICE). The SDG pregnancy group defined two key questions:

a) Use of HbA1c in early pregnancy (booking): For women with “intermediate” HbA1c less than 48mmol/mol but either above normal (42mmol/mol) or at the upper end of normal what is the best management strategy: how great is the risk of GDM in later pregnancy, is this associated with adverse outcomes that might be prevented by glycaemic control?
b) Risk factors for gestational diabetes screening: Should women with previous IUD, PCOS, older age, Chinese/East Asian ethnicity have HbA1c in early pregnancy and later GDM screening with OGTT?

Key question 3: Obstetric members of the SGG pregnancy group have identified key questions as to the best pathways of obstetric care for women with gestational diabetes. It is clear that this is a heterogeneous group ranging from women who will have essentially normal blood glucose after dietary intervention to women with high risk pregnancies. Review of the best strategies to risk stratify women with GDM to different care pathways is required.

5. Areas that will not be covered

Other areas of the existing guideline were felt to be reasonably up to date.

6. Aspects of the proposed clinical topic that are key areas of concern for patients, carers and/or the organisations that represent them

It is a concern to patients and third sector organisations that there is not a unified approach to GDM screening in Scotland. Access to glucose sensing technologies in pregnancy has been a major concern.

7. Population

Included: Pregnant women

Not included:

8. Healthcare setting

Included: Primary and secondary care

Not included.

9. Potential

Potential to improve current practice
The previous SIGN guideline was well received and has been influential in management of women with pre-existing diabetes. Update of sections on glucose sensing technologies will be key in supporting equitable access to these technologies where appropriate. Unifying the approach to screening and diagnosis of GDM is key.

Potential impact on important health outcomes
Pre-existing diabetes- we have good measurement of outcomes including birth weight, stillbirth and gestation at delivery. The purpose of improved glycaemia would be to impact on those outcomes.

Gestational Diabetes: patients are not as easily detectable in routine systems at the moment
but this should be developed in the future.

Potential impact on resources
There is a cost to improved glucose monitoring systems but published studies suggest that these are cost neutral or saving due to reduction in expensive episodes such as neonatal admission.

### 10. What evidence based guidance is currently available?

- None

- **Out-of-date (list)**

- **Current (list)**

### 11. Relevance to current Scottish Government policies

Key questions are in keeping with parts of the current Diabetes Improvement Plan published by Scottish Government (http://www.diabetesinscotland.org.uk/Publications/Diabetes_Improvement_Plan_2014.PDF)

### 12. Who is this guidance for?

- Clinicians involved in care of women with pre-existing diabetes during pregnancy.
- Obstetricians and midwives involved in screening for gestational diabetes.
- Patients in both groups.

### 13. Implementation

**Links with existing audit programmes:** For pre-existing diabetes we are able to audit many outcomes using a combination of existing national diabetes information systems (SCI-Diabetes) and routine data (SMR02). We are interested in and attempting to develop similar outcome systems for gestational diabetes.

**Existing educational initiatives**

**Strategies for monitoring implementation**

### 14. Primary contact for topic proposal

Robert Lindsay (chair SDG pregnancy subgroup)

### 15. Group(s) or institution(s) supporting the proposal

- Scottish Diabetes Group pregnancy subgroup
- Diabetes UK also have representation on the subgroup and are supportive
- The key questions were also partly developed in workshops at the “Improving Diabetes Care” conference run by the Scottish Diabetes Group in February 2018
Having read the SIGN Policy on Declaration of Competing Interests I declare the following competing interests for the previous year, and the following year. I understand that this declaration will be retained by the SIGN Programme Lead and be made available on the SIGN website for time period that the proposal is being considered.

<table>
<thead>
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<th>Signature:</th>
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<table>
<thead>
<tr>
<th>Name:</th>
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<tbody>
<tr>
<td>Robert Lindsay</td>
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<table>
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<tr>
<th>Relationship to SIGN:</th>
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<tbody>
<tr>
<td>Topic proposal primary contact</td>
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<table>
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<td>12/9/2018</td>
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### Personal Interests

**Remuneration from employment**

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<thead>
<tr>
<th>Name of Employer and Post held</th>
<th>Nature of Business</th>
<th>Self or partner/relative</th>
<th>Specific?</th>
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<tbody>
<tr>
<td>University of Glasgow</td>
<td>Clinical care and research</td>
<td>Self</td>
<td>This post includes research into diabetes and pregnancy and clinical care of people with diabetes in and out of pregnancy</td>
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**Remuneration from self employment**

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<th>Name of Business</th>
<th>Nature of Business</th>
<th>Self or partner/relative</th>
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**Remuneration as holder of paid office**

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<th>Organisation</th>
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## Remuneration as a director of an undertaking

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<th>Nature of Business</th>
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<tr>
<td>Details of directorship held which may be significant to, or relevant to, or bear upon the work of SIGN</td>
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## Remuneration as a partner in a firm

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<th>Nature of Business</th>
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<th>Specific?</th>
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<tr>
<td>Details of Partnership held which may be significant to, or relevant to, or bear upon the work of SIGN</td>
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## Shares and securities

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<th>Description of organisation</th>
<th>Description of nature of holding (value need not be disclosed)</th>
<th>Self or partner/relative</th>
<th>Specific?</th>
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<tr>
<td>Details of interests in shares and securities in commercial healthcare companies, organisations and undertakings</td>
<td>None</td>
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## Remuneration from consultancy or other fee paid work commissioned by, or gifts from, commercial healthcare companies, organisations and undertakings

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<th>Nature of work</th>
<th>For whom undertaken and frequency</th>
<th>Self or partner/relative</th>
<th>Specific?</th>
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<tbody>
<tr>
<td>Details of consultancy or other fee paid work which may be significant to, or relevant to, or bear upon the work of SIGN</td>
<td>Previous advisory boards</td>
<td>Eli Lilly and Co Novo Nordisk</td>
<td>Self</td>
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</table>
### Details of gifts which may be significant to, or relevant to, or bear upon the work of SIGN

<table>
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<th>Description of interest</th>
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<th>Specific?</th>
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### Non-financial interests

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<th>Description of interest</th>
<th>Self or partner/ relative</th>
<th>Specific?</th>
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<tbody>
<tr>
<td>Details of non-financial interests which may be significant to, or relevant to, or bear upon the work of SIGN</td>
<td>None</td>
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### Non-personal interests

<table>
<thead>
<tr>
<th>Name of company, organisation or undertaking</th>
<th>Nature of interest</th>
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</thead>
<tbody>
<tr>
<td>Details of non-personal support from commercial healthcare companies, organisations or undertakings</td>
<td>I have acted as PI for studies involving women with diabetes in pregnancy with a mix of commercial (Novo Nordisk) and non-commercial (NIHR EME) sponsors. No personal support for own research form commercial companies</td>
</tr>
</tbody>
</table>

Signature ____________________________ Date: 13/11/2018

Thank you for completing this form.

Please return to
Roberta James
SIGN Programme Lead
SIGN Executive, Healthcare Improvement Scotland,
Gyle Square | 1 South Gyle Crescent | Edinburgh | EH12 9EB

t: 0131 623 4735
e: roberta.james@nhs.net

Data Protection

Your details will be stored on a database for the purposes of managing this guideline topic proposal. We may retain your details so that we can contact you about future Healthcare Improvement Scotland activities. We will not pass these details on to any third parties. Please indicate if you do not want your details to be stored after the proposal is published.
# Initial screen

**Purpose:** initial screening by SIGN Senior Management Team to exclude proposals that are neither clinical, nor multi-professional, nor appropriate for the SIGN process.

| 1. **Is this an appropriate clinical topic for a SIGN guideline?**  
Is it a clinical topic, what is the breadth of the topic and is there a need for the guideline as identified in the proposal? | Yes, it is a request for a small change to the pregnancy section of SIGN 116 on management of diabetes published in 2010. |
|---|---|
| 2. **Is there a suitable alternative product which would address this topic?**  
Would another Healthcare Improvement Scotland product better address the topic? | No |
| 3. **Has this topic been considered before and rejected?**  
What were the reasons for rejection and are they still applicable | No |
| 4. **Outcome** | **YES**  
Go forward to the next stage of topic selection  
Agreed to take forward to GPAG with the proviso that there should be discussion on whether to recommend a refresh of SIGN 116, a short standalone guideline on gestational diabetes or short standalone guideline on pregnancy  
Reject  
**07/02/2018** |
Scope of recent evidence

Summary:

Sixteen guidelines were identified with publication dates ranging from 2008–2019, 3 of which were guidelines/pathways/quality standards from NICE. The guidelines were from the UK, USA, Canada, Qatar and Europe. The following topics were covered in the guidelines:

- management, delivery, and postpartum risk assessment and screening in gestational diabetes
- preconception management
- postpartum management
- obesity in pregnancy
- physical activity in pregnancy.

There is evidence from seven health technology assessments from the UK and North America on:

- countries
- screening and diagnosis of gestational diabetes
- antenatal diet and physical activity
- interventions to reduce or prevent obesity in pregnant women
- screening for hyperglycaemia.

Twenty eight Cochrane reviews provide evidence on interventions for preventing and treating pre-existing and gestational diabetes including:

- screening for risk
- pharmacological therapies
- blood glucose monitoring
- diet
- exercise
- probiotics and supplements
- fetal surveillance
- planned birth
- interconception care

A further 288 systematic reviews were identified.

See Annex 1 for further details
Suitability screen

**Purpose:** screening by the Guideline Programme Advisory Board to select applications suitable for inclusion in the SIGN topic selection process.

<p>| | |</p>
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<tbody>
<tr>
<td>1.</td>
<td><strong>Is there an owner for the project?</strong> (preferably an individual)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>2.</td>
<td><strong>Is this a clinical priority area for NHSScotland?</strong></td>
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<tr>
<td></td>
<td>Yes</td>
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<tr>
<td>3.</td>
<td><strong>Is there a gap between current and optimal practice? OR Is there wide variation in current practice?</strong> (is this an area of clinical uncertainty)</td>
</tr>
<tr>
<td></td>
<td>There are major differences in screening pathways for gestational diabetes between and sometimes within health boards, predominantly relating to which risk factors for GDM prompt screening.</td>
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<tr>
<td>4.</td>
<td><strong>Is there a suitable guideline already available that could be adapted?</strong> (not necessarily by SIGN)</td>
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<td>SIGN 116, published in 2010, on management of diabetes has a chapter on pregnancy. The proposal is to update this section, with the addition of new questions, as a standalone guideline. NICE has updated its guideline on diabetes in pregnancy in 2015.</td>
</tr>
<tr>
<td>5.</td>
<td><strong>Is there adequate literature to make an evidence-based decision about appropriate practice?</strong> (is effective intervention proven and would it reduce mortality or morbidity)</td>
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<tr>
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<td>To be addressed</td>
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<tr>
<td>6.</td>
<td><strong>Would the proposed practice change result in sufficient change in outcomes</strong> (health status, provider and consumer satisfaction and cost) <strong>to justify the effort?</strong></td>
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<tr>
<td></td>
<td>Recommendations to improve glycaemic control would impact on birth weight, stillbirth and gestation at delivery</td>
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<td>How big is the gap?</td>
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<td>How much effort will it take to close the gap?</td>
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<tr>
<td>7.</td>
<td><strong>Is there a perceived need for the guideline, as indicated by a network of relevant stakeholders?</strong></td>
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</table>
|   | Scottish Diabetes Group pregnancy subgroup  
<p>| Diabetes UK also have representation on the subgroup and are supportive |
| 8. | <strong>Is there a reasonable likelihood that NHSScotland could implement the change?</strong> |
|   | Potentially as supported by SDG and in line with Diabetes Improvement Plan published by Scottish Government. For women with pre-existing diabetes outcomes can be audited through existing national diabetes information systems (SCI-Diabetes) and routine data (SMR02). |</p>
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<thead>
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<th>Does the proposer have any conflicts of interest? If so how will these be managed?</th>
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<td>No</td>
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<tr>
<th>10.</th>
<th>Outcome</th>
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<tbody>
<tr>
<td></td>
<td>Go forward to the next stage of topic selection</td>
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<tr>
<td></td>
<td>Reject</td>
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<tr>
<th>11.</th>
<th>Decision</th>
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<td>Ratified by SIGN Council for inclusion on the SIGN guideline development programme</td>
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<th>Comment</th>
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<td>10/10/2018</td>
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</table>
Annex 1 Scope of recent evidence

Topic: diabetes and pregnancy (gestational and pre-existing)

Resources searched:

- GIN (3)
- NICE (3)
- Cochrane Library (28)
- INAHTA (0)
- UKHTA (2)
- EUNetHTA (0)
- Trip Database (2)
- Medline and Embase for SRs ()
- Medline (996), CENTRAL (2394) and Embase (299) for RCTs (numbers only)

Dates searched: searched on 09/10/19 for documents published 2008-2019

Guidelines

Health Technology Assessments


Cochrane reviews


- 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.

Bain E, Crane M, Tieu J, Han S, Crowther CA, Middleton P. Diet and exercise interventions for preventing gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2015;4):CD010443

BACKGROUND: Gestational diabetes mellitus (GDM) is associated with a wide range of adverse health consequences for women and their babies in the short and long term. With an increasing prevalence of GDM worldwide, there is an urgent need to assess strategies for GDM prevention, such as combined diet and exercise interventions.

OBJECTIVES: To assess the effects of combined diet and exercise interventions for preventing GDM and associated adverse health consequences for women and their babies.

SEARCH METHODS: We searched the Cochrane Pregnancy and Childbirth Group’s Trials Register (11 February 2014) and reference lists of retrieved studies. We updated the search in February 2015 but these results have not yet been incorporated and are awaiting classification.

SELECTION CRITERIA: Randomised controlled trials (RCTs) and cluster-RCTs assessing the effects of interventions that included diet and exercise components. We included studies where combined diet and exercise interventions were compared with no intervention (i.e. standard care). We planned to also compare diet and exercise interventions with alternative diet and/or exercise interventions but no trials were identified for this comparison.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed study eligibility, extracted data and assessed the risk of bias of the included studies. Data were checked for accuracy.

MAIN RESULTS: We included 13 randomised controlled trials (involving 4983 women and their babies). We assessed the included trials as being of moderate risk of bias overall. When comparing women receiving a diet and exercise intervention with those receiving no intervention, there was no clear difference in the risk of developing GDM (average risk ratio (RR) 0.92, 95% confidence interval (CI) 0.68 to 1.23; 11 trials, 3744 women), caesarean section (RR 0.92, 95% CI 0.83 to 1.01; seven trials, 3246 women), or large-for-gestational age (RR 0.90, 95% CI 0.77 to 1.05; 2950 infants). Only one trial reported on perinatal mortality, and found no clear difference in the risk of stillbirth (RR 0.99, 95% CI 0.29 to 3.42; 2202 fetuses) or neonatal death (RR 0.99, 95% CI 0.06 to 15.85; 2202 neonates). Very few differences were shown between groups for the review's secondary outcomes, including for induction of labour, perineal trauma, pre-eclampsia, postpartum haemorrhage and infection, macrosomia, birthweight, small-for-gestational age, ponderal index, neonatal hypoglycaemia requiring treatment, hyperbilirubinaemia requiring treatment, shoulder dystocia, bone fracture or nerve palsy. Women receiving a combined diet and exercise intervention were, however, found to have a reduced risk of preterm birth compared with women receiving no intervention (RR 0.71, 95% CI 0.55 to 0.93; five trials, 2713 women). A trend towards reduced weight gain during pregnancy was shown for women receiving the combined diet and exercise intervention (mean difference (MD) -0.76 kg, 95% CI -1.55 to 0.03; eight trials, 2707 women; P = 0.06, random-effects); but no clear difference in postnatal weight retention was observed overall. In relation to adherence to the interventions, a number of trials that reported on behaviour modifications showed benefits in diet- (5/8 trials) and physical activity- (4/8 trials) related behaviours for women receiving the combined diet and exercise intervention, compared with women receiving no intervention; however there was notable variation across trials in outcomes measured and results observed. Only two trials reported on well-being and quality of life of women, and did not observe differences between groups for these outcomes. Very few trials reported on outcomes relating to the use of health services, although one trial suggested a reduced length of antenatal hospital stay for women receiving a combined diet and exercise intervention (MD -0.27 days, 95% CI -0.49 to -0.05; 2153 women). No information was available on outcomes for the infant as a child or adult, or for most longer-term outcomes for the mother.

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AUTHORS' CONCLUSIONS: There are limitations associated with the available RCT evidence on the effects of combined diet and exercise interventions during pregnancy for preventing GDM. Results from 13 RCTs (of moderate quality) suggest no clear difference in the risk of developing GDM for women receiving a combined diet and exercise intervention compared with women receiving no intervention. However, the ability to draw firm conclusions was limited by variations in the quality of trials, characteristics of the interventions and populations assessed, and outcome definitions between trials. Based on the data currently available, conclusive evidence is not available to guide practice. Further large, well-designed RCTs, addressing the limitations of previous studies, are needed to assess the effects of combined interventions on preventing GDM and other relevant pregnancy outcomes including caesarean birth, large-for-gestational age and perinatal mortality. Health service utilisation and costs, and longer-term outcomes for mothers and their babies should be included. We identified another 16 trials which are ongoing and we will consider these for inclusion in the next update of this review.


- Background Gestational diabetes mellitus (GDM) is associated with a range of adverse pregnancy outcomes for mother and infant. The prevention of GDM using lifestyle interventions has proven difficult. The gut microbiome (the composite of bacteria present in the intestines) influences host inflammatory pathways, glucose and lipid metabolism and, in other settings, alteration of the gut microbiome has been shown to impact on these host responses. Probiotics are one way of altering the gut microbiome but little is known about their use in influencing the metabolic environment of pregnancy. Objectives To assess the effects of probiotic supplementation when compared with other methods for the prevention of GDM. Search methods We searched the Cochrane Pregnancy and childbirth Group's Trials Register (31 August 2013) and reference lists of the articles of retrieved studies. Selection criteria Randomised and cluster-randomised trials comparing the use of probiotic supplementation with other methods for the prevention of the development of GDM. Cluster-randomised trials were eligible for inclusion but none were identified. Quasi-randomised and cross-over design studies are not eligible for inclusion in this review. Studies presented only as abstracts with no subsequent full report of study results would also have been excluded. Data collection and analysis Two review authors independently assessed study eligibility, extracted data and assessed risk of bias of included study. Data were checked for accuracy. Main results Eleven reports (relating to five possible trials) were found. We included one study (six trial reports) involving 256 women. Four other studies are ongoing. The included trial consisted of three treatment arms: probiotic with dietary intervention, placebo and dietary intervention, and dietary intervention alone; it was at a low risk of bias. The study reported primary outcomes of a reduction in the rate of gestational diabetes mellitus (risk ratio (RR) 0.38, 95% confidence interval (CI) 0.20 to 0.70), with no statistical difference in the rates of miscarriage/intrauterine fetal death (IUD) stillbirth/neonatal death (RR 2.00, 95% CI 0.35 to 11.35). Secondary outcomes reported were a reduction in infant birthweight (mean difference (MD) -127.71 g, 95% CI -251.37 to -4.06) in the probiotic group and no clear evidence of increased risk of preterm delivery (RR 3.27, 95% CI 0.44 to 24.43), or caesarean section rate (RR 1.23, 95% CI 0.65 to 2.32). The primary infant outcomes of rates of macrosomia and large-for-gestational age infants were not reported. The following secondary outcomes were not reported: maternal gestational weight gain, pre-eclampsia, and the long-term diagnosis of diabetes mellitus; infant body composition, shoulder dystocia, admission to neonatal intensive care, jaundice, hypoglycaemia and long-term rates of obesity and diabetes mellitus. Authors' conclusions One trial has shown a reduction in the rate of GDM when women are randomised to probiotics early in pregnancy but more uncertain evidence of any effect on miscarriage/IUD stillbirth/neonatal death. There are no data on macrosomia. At this time, there are insufficient studies to perform a quantitative meta-analysis. Further results are awaited from four ongoing studies. Plain language summary Probiotics to prevent gestational diabetes mellitus Gestational diabetes mellitus is a condition where the mother has high blood sugar levels during pregnancy. It is associated with a range of adverse pregnancy outcomes for the mother, such as pre-eclampsia (high blood pressure with protein in the urine) and instrumental or operative delivery, as well as for the infants who may be born large-for-gestational age. Current treatment includes diet with or without medication. Prevention of this condition would be preferable to treatment. Preventative diet and lifestyle interventions are time consuming and do not always reduce the number of women getting gestational diabetes. Probiotics - 'good' bacteria that are usually taken in the form of capsules or drinks - supplement the gut bacteria. They have the potential to change a person's metabolism and so prevent gestational diabetes mellitus. This review was designed to look at whether there is evidence to show if this is true or not. At the moment there is only one randomised controlled study, which involved 256 women. This study does show a lower rate of gestational diabetes mellitus in women who took probiotics from early pregnancy, with the rate of diagnosis of gestational diabetes mellitus
being reduced by two-thirds and their babies on average weighed 127 g less at birth. This study did not find differences in the rates of miscarriage, intrauterine or neonatal death or stillbirth. There was no clear evidence of a change in the proportion of women delivered by caesarean section or in the risk of preterm delivery. The study did not report on how much weight the mothers gained during pregnancy or how many babies were large-for-gestational age or that weighed more than 4000 g at birth or on the body composition of the babies. One study is not enough to draw any definite conclusions at the moment. There are other studies underway.


- Background Gestational diabetes is a type of diabetes that occurs during pregnancy. Women with gestational diabetes are more likely to experience adverse health outcomes such as pre-eclampsia or polyhydramnios (excess amniotic fluid). Their babies are also more likely to have health complications such as macrosomia (birthweight > 4000 g) and being large-for-gestational age (birthweight above the 90th percentile for gestational age). Current clinical guidelines support elective birth, at or near term in women with gestational diabetes to minimise perinatal complications, especially those related to macrosomia. This review replaces a review previously published in 2001 that included “diabetic pregnant women”, which has now been split into two reviews. This current review focuses on pregnant women with gestational diabetes and a sister review focuses on women with pre-existing diabetes (Type 1 or Type 2). Objectives To assess the effect of planned birth (either by induction of labour or caesarean birth), at or near term (37 to 40 weeks’ gestation) compared with an expectant approach for improving health outcomes for women with gestational diabetes and their infants. The primary outcomes relate to maternal and perinatal mortality and morbidity. Search methods We searched Cochrane Pregnancy and Childbirth’s Trials Register, ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) (15 August 2017), and reference lists of retrieved studies. Selection criteria We included randomised trials comparing planned birth, at or near term (37 to 40 weeks’ gestation), with an expectant approach, for women with gestational diabetes. Cluster-randomised and non-randomised trials (e.g. quasi-randomised trials using alternate allocation) were also eligible for inclusion but none were identified. Data collection and analysis Two of the review authors independently assessed study eligibility, extracted data and assessed the risk of bias of the included study. The quality of the evidence was assessed using the GRADE approach. Main results The findings of this review are based on a single trial involving 425 women with gestational diabetes. The trial compared induction of labour with expectant management (waiting for the spontaneous onset of labour in the absence of any maternal or fetal issues that may necessitate birth) in pregnant women with gestational diabetes at term. We assessed the overall risk of bias as being low for most domains, apart from performance, detection and attrition bias (for outcome perineum intact), which we assessed as being at high risk. It was an open-label trial, and women and healthcare professionals were not blinded. There were no clear differences between women randomised to induction of labour and women randomised to expectant management for maternal mortality or serious maternal morbidity (risk ratio (RR) 1.48, 95% confidence interval (CI) 0.25 to 8.76, one trial, 425 women); caesarean section (RR 1.06, 95% CI 0.64 to 1.77, one trial, 425 women); or instrumental vaginal birth (RR 0.81, 95% CI 0.45 to 1.46, one trial, 425 women). For the primary outcome of maternal mortality or serious maternal morbidity, there were no deaths in either group and serious maternal morbidity related to admissions to intensive care unit. The quality of the evidence contributing to these outcomes was assessed as very low, mainly due to the study having high risk of bias for some domains and because of the imprecision of effect estimates. In relation to primary neonatal outcomes, there were no perinatal deaths in either group. The quality of evidence for this outcome was judged as very low, mainly due to high risk of bias and imprecision of effect estimates. There were no clear differences between women randomised to induction of labour and women randomised to expectant management: shoulder dystocia (RR 2.96, 95% CI 0.31 to 28.21, one trial, 425 infants, very low-quality evidence); large-for-gestational age (RR 0.53, 95% CI 0.28 to 1.02, one trial, 425 infants, low-quality evidence). There were no clear differences between women randomised to induction of labour and women randomised to expectant management for postpartum haemorrhage (RR 1.17, 95% CI 0.53 to 2.54, one trial, 425 women); admission to intensive care unit (RR 1.48, 95% CI 0.25 to 8.76, one trial, 425 women); and intact perineum (RR 1.02, 95% CI 0.73 to 1.43, one trial, 425 women). No infant experienced a birth trauma, therefore, we could not draw conclusions about the effect of the intervention on the outcomes of brachial plexus injury and bone fracture at birth. Infants of women in the induction-of-labour group had higher incidences of neonatal hyperbilirubinaemia (jaundice) when compared to infants of women in the expectant-management group (RR 2.46, 95% CI 1.11 to 5.46, one trial, 425 women). We found no data on the following prespecified outcomes of this review: postnatal depression, maternal satisfaction, length of postnatal stay (mother), acidemia, intracranial haemorrhage, hypoxia ischaemic encephalopathy, small-for-gestational age, length of postnatal stay (baby) and cost. The authors of this trial acknowledge that it is underpowered for their primary outcome of caesarean section. The
Background Gestational diabetes (GDM) is glucose intolerance, first recognised in pregnancy and usually resolving after birth. GDM is associated with both short- and long-term adverse effects for the mother and her infant. Lifestyle interventions are the primary therapeutic strategy for many women with GDM. Objectives To evaluate the effects of combined lifestyle interventions with or without pharmacotherapy in treating women with gestational diabetes. Search methods We searched the Pregnancy and Childbirth Group's Trials Register (14 May 2016), ClinicalTrials.gov, WHO International Clinical Trials Registry Platform (ICTRP) (14th May 2016) and reference lists of retrieved studies. Selection criteria We included only randomised controlled trials comparing a lifestyle intervention with usual care or another intervention for the treatment of pregnant women with GDM. Quasi-randomised trials were excluded. Cross-over trials were not eligible for inclusion. Women with pre-existing type 1 or type 2 diabetes were excluded. Data collection and analysis We used standard methodological procedures expected by the Cochrane Collaboration. All selection of studies, data extraction was conducted independently by two review authors. Main results Fifteen trials (in 45 reports) are included in this review (4501 women, 3768 infants). None of the trials were funded by a conditional grant from a pharmaceutical company. The lifestyle interventions included a wide variety of components such as education, diet, exercise and self-monitoring of blood glucose. The control group included usual antenatal care or diet alone. Using GRADE methodology, the quality of the evidence ranged from high to very low quality. The main reasons for downgrading evidence were inconsistency and risk of bias. We summarised the following data from the important outcomes of this review. Lifestyle intervention versus control group For the mother: There was no clear evidence of a difference between lifestyle intervention and control groups for the following outcomes: postnatal stay, babies with high blood acid, bleeding in the baby's brain, other brain problems for the babies, babies small-for-gestational age and length of baby's postnatal stay. What does this mean? There is insufficient evidence to clearly identify if there are differences in health outcomes for women with gestational diabetes and their babies when elective birth is undertaken compared to waiting for labour to start spontaneously or until 41 weeks' gestation if all is well. More research is needed to answer this question.

Diabetes during pregnancy has been linked to many short-term risks for the infants. Plain language summary Lifestyle interventions for treating women with gestational diabetes (or diabetes in pregnancy) are useful as the primary therapeutic strategy and most commonly included healthy eating, activity, education, and self-management of blood glucose concentrations. Future research could focus on which specific interventions are most useful (as the sole intervention without pharmacological treatment), which health professionals should give them and the optimal format for providing the information. Evaluation of long-term outcomes for the mother and her child should be a priority when planning future trials. There has been no in-depth exploration of the costs ‘saved’ from reducing the risk of LGA/macrosomia and potential longer-term risks for the infants. Plain language summary Lifestyle interventions for treating women with gestational diabetes (or diabetes in pregnancy) What is the issue? Gestational diabetes (GDM), is a glucose intolerance leading to high blood glucose levels that is first recognised during pregnancy and which usually normalises after giving birth. Diabetes during pregnancy has been linked to many short-term and long-term health problems for the mother and her baby. The main way to treat GDM is through lifestyle changes such as diet, exercise and checking blood glucose levels. Why is this important? Women with GDM have an increased risk of developing high blood pressure during pregnancy (pre-eclampsia) and are more likely to have their labour induced. The babies of women with GDM are more likely to be large when born and this can be linked to babies having birth trauma (bones broken or nerves damaged during the birth) and the need for giving birth by caesarean section. Lifestyle interventions that include two or more components of dietary advice, physical activity, education, and self-monitoring of blood glucose are the first-line treatment for most women diagnosed with GDM. Interventions such as healthy eating and physical activity aim to help women maintain their blood glucose levels within a target range and to improve health outcomes for the mother and baby. What evidence did we find? We searched the literature (May 2016) for controlled trials comparing lifestyle intervention with a control group of women receiving usual care or another intervention. Fifteen randomised controlled trials (45 publications) are included in this review, involving 4501 women and 3768 infants. None of the trials were funded by a conditional grant from a pharmaceutical company. For the baby, lifestyle interventions were associated with a reduction in the risk of being born large-for-gestational age (six trials, 2994 infants). The number of babies with birthweight over 4000 g (macrosomia) was lower with the lifestyle intervention, with no clear difference in the number of newborn babies experiencing low blood glucose levels (six trials, 3000 infants).
infants). The evidence was of moderate quality for these findings. Birthweight was also lower in the lifestyle intervention group. For the mothers, introducing lifestyle interventions made no clear difference in the number of women with pregnancy-induced high blood pressure (four trials, 2796 women) or having a caesarean section (10 trials, 3545 women) based on low-quality evidence or on induction of labour (four trials, 2699 women, high-quality evidence). Similar numbers of women experienced perineal trauma or tearing (one trial, 1000 women) or developed type 2 diabetes at a maximum of 10 years after giving birth (two trials, 486 women). These findings were supported by low- to moderate-quality evidence. More women in the lifestyle group had met their weight goals one year after giving birth, and lifestyle interventions were associated with a decrease in the risk of depression after birth, from single trials. These findings were supported by low quality evidence. What does this mean? Lifestyle interventions provide benefits to women with GDM and their babies. The interventions are useful as the primary therapeutic strategy and generally include, as a minimum, healthy eating, physical activity and self-monitoring of blood sugar levels. Further research could focus on the effective components of lifestyle interventions and the use of lifestyle interventions as the sole intervention without pharmacological treatment. Future studies also need to consider long-term outcomes for the mother and her child as a priority when planning future trials.

Brown J, CeySENS G, BouLVAIN M. Exercise for pregnant women with gestational diabetes for improving maternal and fetal outcomes. Cochrane Database of Systematic Reviews 2017;6: - Background Gestational diabetes mellitus (GDM) is associated with both short- and long-term complications for the mother and her baby. Exercise interventions may be useful in helping with glycaemic control and improve maternal and infant outcomes. The original review on Exercise for diabetic pregnant women has been split into two new review titles reflecting the role of exercise for pregnant women with gestational diabetes and for pregnant women with pre-existing diabetes. Exercise for pregnant women with gestational diabetes for improving maternal and fetal outcomes (this review) Exercise for pregnant women with pre-existing diabetes for improving maternal and fetal outcomes Objectives To evaluate the effects of exercise interventions for improving maternal and fetal outcomes in women with GDM. Search methods We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (27 August 2016), ClinicalTrials.gov , the WHO International Clinical Trials Registry Platform (ICTRP ) (18th August 2016), and reference lists of retrieved studies. Selection criteria We included randomised controlled trials (RCTs) comparing an exercise intervention with standard care or another intervention in pregnant women diagnosed with gestational diabetes. Quasi-randomised and cross-over studies, and studies including women with pre-existing type 1 or type 2 diabetes were not eligible for inclusion. Data collection and analysis All selection of studies, assessment of trial quality and data extraction was conducted independently by two review authors. Data were checked for accuracy. Main results We included 11 randomised trials, involving 638 women. The overall risk of bias was judged to be unclear due to lack of methodological detail in the included studies. For the mother, there was no clear evidence of a difference between women in the exercise group and those in the control group for the risk of pre-eclampsia as the measure of hypertensive disorders of pregnancy (risk ratio (RR) 0.31, 95% confidence interval (CI) 0.01 to 7.09; two RCTs, 48 women; low-quality evidence) , birth by caesarean section (RR 0.86, 95% CI 0.63 to 1.16; five RCTs, 316 women; I 2 = 0%; moderate-quality evidence) , the risk of induction of labour (RR 1.38, 95% CI 0.71 to 2.68; one RCT, 40 women; low-quality evidence) or maternal body mass index at follow-up (postnatal weight retention or return to pre-pregnancy weight) (mean difference (MD) 0.11 kg/m 2 , 95% CI -1.04 to 1.26; three RCTs, 254 women; I 2 = 0%; high-quality evidence). Development of type 2 diabetes, perineal trauma/tearing and postnatal depression were not reported as outcomes in the included studies. For the infant/child/adult, a single small (n = 19) trial reported no perinatal mortality (stillbirth and neonatal mortality) events in either the exercise intervention or control group (low-quality evidence). There was no clear evidence of a difference between groups for a mortality and morbidity composite (variously defined by trials, e.g. perinatal or infant death, shoulder dystocia, bone fracture or nerve palsy) (RR 0.56, 95% CI 0.12 to 2.61; two RCTs, 169 infants; I 2 = 0%; moderate-quality evidence) or neonatal hypoglycaemia (RR 2.00, 95% CI 0.20 to 20.04; one RCT, 34 infants; low-quality evidence). None of the included trials pre-specified large-for-gestational age, adiposity (neonatal/infant, childhood or adulthood), diabetes (childhood or adulthood) or neurosensory disability (neonatal/infant) as trial outcomes. Other maternal outcomes of interest: exercise interventions were associated with both reduced fasting blood glucose concentrations (average standardised mean difference (SMD) -0.59, 95% CI -1.07 to -0.11; four RCTs, 363 women; I 2 = 73%; T 2 = 0.19) and a reduced postprandial blood glucose concentration compared with control interventions (average SMD -0.85, 95% CI -1.15 to -0.55; three RCTs, 344 women; I 2 = 34%; T 2 = 0.03). Author ‘ conclusions Short- and long-term outcomes of interest for this review were poorly reported. Current evidence is confounded by the large variety of exercise interventions. There was insufficient high-quality evidence to be able to determine any differences between exercise and control groups for our outcomes of interest. For the woman, both fasting and postprandial blood glucose concentrations were reduced compared with the control groups. There are
currently insufficient data for us to determine if there are also benefits for the infant. The quality of the evidence in this review ranged from high to low quality and the main reason for downgrading was for risk of bias and imprecision (wide CIs, low event rates and small sample size). Development of type 2 diabetes, perineal trauma/tearing, postnatal depression, large-for-gestational age, adiposity (neonate/infant, childhood or adulthood), diabetes (childhood or adulthood) or neurosensory disability (neonate/infant) were not reported as outcomes in the included studies. Further research is required comparing different types of exercise interventions with control groups or with another exercise intervention that reports on both the short- and long-term outcomes (for both the mother and infant/child) as listed in this review. Plain language summary Can exercise, for women with gestational diabetes, improve outcomes for mother and her baby? What is the issue? A previous Cochrane review on Exercise for diabetic pregnant women included women with pre-existing diabetes and women with gestational diabetes. That review has now been split into two new reviews on: exercise for pregnant women with gestational diabetes (this review) and exercise for pregnant women with pre-existing diabetes (the subject of another new review). There will be similarities in the background, methods and outcomes between these two systematic reviews. Gestational diabetes mellitus (GDM), or diabetes during pregnancy, has both short- and long-term complications for the mother and her baby. Women with GDM are at an increased chance of developing high blood pressure or pre-eclampsia during pregnancy, having their labour induced, giving birth by caesarean section, and experiencing perineal trauma. In the long term, up to half of women with GDM are likely to develop type 2 diabetes. Their babies are at increased risk of being born large-for-gestational age, experiencing a birth injury and being admitted to the neonatal intensive care unit. They are also more likely to develop metabolic syndrome in childhood and later life. Why is this important? Exercise may help to control blood sugar levels and improve outcomes for the mother and her baby, possibly leading to long-term health benefits. Physical activity for this review is planned, structured and repetitive body movements undertaken to improve physical fitness. What evidence did we find? We searched for evidence from randomised controlled trials in August 2016. We identified 11 trials that involved 638 pregnant women. They were conducted in middle- or high-income countries. We judged the overall risk of bias in the trials as unclear because of a lack of information about how the trials were conducted. Using GRADE, the quality of the evidence from the trials ranged from high to low quality. The main reasons for downgrading the quality were for risk of bias in the trials and imprecise effect sizes, low event rates and small numbers of participants. For the mothers, exercising did not appear to reduce the risk of pre-eclampsia as the measure of hypertensive disorders of pregnancy (two trials, 48 women, low-quality evidence), birth by caesarean section (five trials, 316 women, moderate-quality evidence), or the risk of induction of labour (one trial, 40 women, low-quality evidence). The mothers had similar body mass index at follow-up in the exercise and control groups (three trials, 254 women, high-quality evidence). Exercise was associated with lower fasting blood glucose levels (four trials) and blood glucose levels after a meal (three trials) but with variations in effect sizes between the different trials. The exercise programmes varied between trials as did their duration and whether or not they were supervised. None of the included trials reported on perineal trauma, postnatal depression or development of type 2 diabetes. For the babies, no deaths occurred around the time of birth in (one trial, 19 babies, low-quality evidence) and there was no evidence of any difference in the risk of ill-health (two trials, 169 babies, moderate-quality evidence) or low blood sugar levels (one trial, 34 babies, low-quality evidence). None of the trials reported on the number of large-for-gestational-age babies or babies that went on to develop diabetes in childhood or adulthood or neurosensory disability that became apparent during childhood. What does this mean? Although exercise appeared to be able to lower fasting blood sugar levels and sugar levels after a meal, we did not find any differences in other outcomes for pregnant women with GDM. The present evidence is insufficient to advise for or against women enrolling in exercise programmes. Even if exercise does not provide any benefit during pregnancy, this change in lifestyle may persist after birth and may help prevent the onset of type 2 diabetes and its long-term complications. Pregnant women with GDM who wish to enrol in an exercise programme may wish to discuss their choice with a health professional. Further research is needed comparing one exercise intervention with another (or with a control) and reporting on both the short- and long-term outcomes (for both the mother and infant/child/adult) as listed in this review.

Brown J, Ceysens G, Boulvain M. Exercise for pregnant women with pre-existing diabetes for improving maternal and fetal outcomes. Cochrane Database of Systematic Reviews 2017;12): - Background Pregnanacies with pre-existing diabetes are high risk, with increased risk of poorer fetal, neonatal, and maternal outcomes. Identifying interventions to improving health outcomes for women with diabetes and their infants is a priority, as rates of diabetes continue to increase. Exercise has been shown to have benefits for non-pregnant individuals with pre-existing type 2 diabetes, such as improving glycaemic control, and reducing visceral adipose tissue and plasma triglycerides. For pregnant women with pre-existing diabetes, the effects of exercise interventions on the mother and her baby are unknown. An earlier Cochrane review on ‘Exercise for pregnant women with diabetes’ considered both pre-existing diabetes and gestational diabetes. That Cochrane review has now been split into two new reviews (following new protocols) - one on
gestational diabetes and one on pre-existing diabetes (this review). Objectives To evaluate the effects of exercise interventions for improving maternal and fetal outcomes in women with pre-existing diabetes. Search methods We searched Cochrane Pregnancy and Childbirth’s Trials Register, ClinicalTrials.gov, and the WHO International Clinical Trials Registry Platform (ICTRP) on 27 June 2017, and reference lists of retrieved studies. Selection criteria We had planned to include published or unpublished randomised controlled trials (RCT) or cluster-randomised trials, in full text or abstract format that compared any type of exercise programme, added to standard care, targeted at women with known pre-gestational diabetes (type 1 or type 2 diabetes), at any stage of pregnancy, compared with 1) standard care alone or 2) standard care plus another exercise intervention. Quasi-randomised and cross-over trials were excluded. Conference abstracts were handled in the same way as full-text publications. Women with gestational diabetes mellitus were excluded, as they were covered in a separate Cochrane review. Data collection and analysis We had planned that two review authors would independently assess all the potential studies we identified as a result of the search strategy. For eligible studies, two review authors would have independently extracted the data using an agreed form. We had planned to resolve discrepancies through discussion, or by consulting a third person. We also had planned to assess the evidence using the GRADE approach. Main results We did not identify any randomised controlled trials. Authors’ conclusions There was no evidence from RCTs that evaluated the effects of exercise interventions for improving maternal and fetal outcomes in women with pre-existing diabetes. Good quality, large randomised controlled trials are urgently needed to identify exercise interventions that are safe, and improve health outcomes for women with pre-existing diabetes and their babies. Future studies in this area could utilise the standardised outcomes in this review, in order to improve consistency between trials in this area, and aid future meta-analysis. Plain language summary Exercise for improving outcomes for women with pre-existing diabetes and their babies What is the issue? Diabetes mellitus can be caused by autoimmune destruction of the cells producing insulin, so that levels are reduced (type 1 diabetes), or the body tissues becoming resistant to insulin (type 2 diabetes). The end result is increased blood glucose levels. Insulin is used to regulate glucose levels for pregnant women with type 1 diabetes. For women with type 2 diabetes, lifestyle changes, including diet and exercise, are an important part of treatment. An oral anti-diabetic drug (medication that aims to reduce blood sugar levels) or insulin may be added to lower blood glucose levels. We set out to evaluate the effects of exercise interventions, for pregnant women with pre-existing type 1 or 2 diabetes, on birth outcomes for the mother and her baby. An earlier review on the effects of exercise on diabetes during pregnancy has been split into two reviews - one for women with gestational diabetes, and this review, on women with pre-existing diabetes. Why is this important? Women with diabetes, who become pregnant, are at increased risk of pregnancy loss, or having a baby that is large-for-gestational age (baby is larger than would be expected for the number of weeks of pregnancy), is born preterm, who dies around the time of birth, or is born with birth defects. The newborn baby may also have blood sugar levels that are lower than normal, low calcium levels, and excess bilirubin in the blood. Long-term follow-up of the infants of diabetic mothers suggests that they are at increased risk of obesity and type 2 diabetes when older. The number of women who already have diabetes when they become pregnant is increasing, and identifying ways to improve health outcomes for women with diabetes and their babies is a priority. We already know that exercise may be of benefit for non-pregnant women with type 2 diabetes, as it improves their blood glucose levels and reduces triglyceride fats in the blood. We are unclear if exercise benefits, and is safe for, pregnant women with pre-existing diabetes and their babies. Physical activity could help to increase fitness and prevent stress urinary incontinence, lower back pain, or depression, and control weight gain during pregnancy. What evidence did we find? We searched for evidence on 27 June 2017. We did not identify any randomised controlled trials (RCT) that compared any type of exercise programme (plus standard care) for pregnant women with pre-existing diabetes with 1) standard care alone, or 2) standard care plus another exercise programme. What does this mean? There is no evidence from RCTs to evaluate the effects of exercise interventions for improving mother and baby outcomes in women with pre-existing diabetes. Good quality, large studies are urgently needed to find out if exercise interventions are safe, and if they improve health outcomes for pregnant women with diabetes and their babies. Future studies in this area could utilise the outcomes listed in this review, to improve consistency between trials in this area, and aid future analyses.

- Background Gestational diabetes mellitus (GDM) is any degree of glucose intolerance that first presents and is recognised during pregnancy and usually resolves after the birth of the baby. GDM is associated with increased short- and long-term morbidity for the mother and her baby. Treatment usually includes lifestyle modification and/or pharmacological therapy (oral antidiabetic agents or insulin) with the aim to maintain treatment targets for blood glucose concentrations. Finding novel treatment agents which are effective, acceptable and safe for the mother and her baby are important. One such emerging potential intervention is
myo-inositol which is an isomer of inositol and occurs endogenously and is found in natural dietary sources such as fruits, vegetables, nuts and cereals. Objectives To assess if dietary supplementation with myo-inositol during pregnancy is safe and effective, for the mother and fetus, in treating gestational diabetes. Search methods We searched the Cochrane Pregnancy and Childbirth Group’s Trials Register (30 April 2016), ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) (7 April 2016), and reference lists of retrieved studies. Selection criteria All published and unpublished randomised controlled trials or cluster-randomised controlled trials reporting on the use of myo-inositol compared with placebo, no treatment or another intervention for the treatment of women with gestational diabetes. Quasi-randomised and cross-over studies are not eligible for inclusion. Women with pre-existing diabetes were excluded. Data collection and analysis Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. For key outcomes (where data were available), we assessed the quality of the evidence using the GRADE approach. Main results We included two studies (142 women and infants), both were conducted in women in Italy and compared myo-inositol with a placebo control. None of the maternal primary outcomes pre-specified for this review were reported in the included studies: hypertensive disorders of pregnancy; caesarean section; development of subsequent type 2 diabetes mellitus. No data were reported for the majority of this review's maternal secondary outcomes. We could only perform meta-analysis for two secondary outcomes: fasting oral glucose tolerance test and additional pharmacological treatment. All other results are based on data from single studies. Overall, the risk of bias of the included studies was judged to be unclear due to lack of key methodological information. There was no evidence of a difference between treatment groups in need for additional pharmacotherapy or weight gain during pregnancy, although myo-inositol was associated with a lower body mass index (BMI) change (mean difference (MD) -1.50 kg/m²; 95% confidence interval (CI) -2.35 to -0.65; one trial, n = 73). Myo-inositol was associated with a reduction in the fasting blood glucose concentration at the end of treatment (MD -0.47 mmol/L; 95% CI -0.59 to -0.35; two trials, n = 142 women) compared with the control group. One small trial reported that myo-inositol was associated with a reduction in one-hour post-prandial blood glucose concentration at the end of treatment (MD -0.90 mmol/L; 95% CI -1.73 to -0.07; one trial, n = 73 women) compared with the control group. There was no difference between groups for the two-hour post-prandial blood glucose concentrations between groups (MD -0.70 mmol/L; 95% CI -1.46 to 0.06; one trial, n = 73 women). The one-hour and two-hour blood glucose concentrations show evidence of imprecision associated with wide CIs and small sample size. For the infant, there was no evidence of a difference in the risk for being born large-for-gestational age between the myo-inositol and the control group (risk ratio (RR) 0.36; 95% CI 0.02 to 8.58; one trial, n = 73 infants; low-quality evidence). The evidence was downgraded due to imprecision. This review's other primary outcomes were not reported in the included trials: perinatal mortality (stillbirth and neonatal mortality); mortality of morbidity composite (as defined by the trials); neurosensory disability. Infants in the myo-inositol group were less likely to have neonatal hypoglycaemia compared with the placebo group (RR 0.05; 95% CI 0.00 to 0.85; one study, n = 73 infants; low-quality evidence). There is evidence of imprecision for this outcome with low event rates and small sample size. There was no evidence of a difference between treatment and placebo groups for preterm birth or birthweight. Myo-inositol was associated with a later gestational age at birth compared with the placebo group (MD 2.10 weeks; 95% CI 1.27 to 2.93; one trial, n = 73 infants). No data were reported for any of the other neonatal outcomes for this review. No long-term outcomes were reported for the mother, infant as a child, infant as an adult, or health service outcomes. Authors' conclusions There are insufficient data to evaluate the effect of myo-inositol for the treatment of gestational diabetes, without any data to examine the majority of outcomes in this review. There do not appear to be any benefits for the infant associated with exposure to myo-inositol such as reduced risk of being born large-for-gestational age. Although the risk of neonatal hypoglycaemia is reduced for the myo-inositol group, there is evidence of imprecision. Evidence from two studies suggested that myo-inositol was associated with a reduced change in maternal BMI and fasting blood sugar concentration compared with placebo. There is a lack of reporting of the clinically meaningful outcomes pre-specified for this review. Uncertainty of the effectiveness of myo-inositol as a treatment for GDM for key maternal and infant outcomes remains and further high-quality trials with appropriate sample sizes are required to further investigate the role of myo-inositol as a treatment or co-treatment for women with gestational diabetes. Future trials should report on the core outcomes for GDM identified in the methods section of this review. Participants of varying ethnicities and with varying risk factors for GDM should be included in future trials. In addition, further trials of myo-inositol for the treatment of GDM should explore the optimal dose, frequency and timing of supplementation, report on adverse effects and assess the long-term effects of this intervention. Economic analysis or health service use and costs should also be included. Plain language summary Does taking a supplement of myo-inositol work as an effective treatment for women who develop diabetes during pregnancy? What is the issue? During pregnancy the mother develops resistance to insulin and the uptake of glucose from the blood is reduced to ensure the baby has a consistent supply of glucose. The mother has to produce extra insulin to keep her blood glucose levels under control or she is at risk of developing gestational
diabetes mellitus (GDM). GDM is diabetes that occurs during pregnancy and resolves after birth of the baby. It is an increasing problem around the world, causing both long- and short-term complications for the mother and her baby. Women with GDM are at greater risk of developing high blood pressure and having a caesarean section for the birth. Their babies can grow large for their gestational age, which increases the likelihood of having an injury at birth such as broken bones or a shoulder becoming stuck. In the long term both the mother and her child are at increased risk of developing type 2 diabetes. Why is this important? Dietary and lifestyle counselling is the first line of treatment for women with GDM. An oral hypoglycaemic drug or insulin therapy is recommended for the women who are still unable to maintain target blood glucose levels. Finding a treatment that controls the mother’s blood sugar levels without harming the mother or her baby is important. Myo-inositol is a natural form of inositol that is found in fruits, vegetables, nuts and cereals. It is a simple carbohydrate nutrient the body requires for many cell functions. Myo-inositol is available as a dietary supplement, in water-soluble powder form or as capsules. What evidence did we find? We searched for evidence in April 2016 and identified two randomised controlled studies (involving 142 women and their babies). Both studies were conducted in Italy (and were judged to be at an unclear risk of bias). The women were diagnosed with GDM at 12 to 13 weeks’ gestation in one study and at 26 weeks’ gestation in the other. The findings from these trials suggested that myo-inositol can reduce fasting blood glucose levels. The need for supplementary insulin was not clearly different between the women receiving myo-inositol and the control groups. One of the studies showed reduced glucose levels at one hour after a meal (one study, 73 women) There was no evidence to suggest that the babies were at reduced risk of being born large-for-gestational age (one study, 73 infants). Myo-inositol appeared to reduce the risk of the baby having low blood sugar levels at birth and being born at a later gestational age, although the evidence was of low quality. Many of the infant and maternal outcomes identified as being of interest for this review were not reported in the included studies - these included: high blood pressure during the pregnancy, caesarean section, the development of type 2 diabetes (maternal), and the number of babies who died or were unwell, or the number of babies with neurosensory disability. No long-term outcomes were reported for the mother, infant as a child, infant as an adult or health service outcomes. What does this mean? Because of the limited number of studies reporting on myo-inositol for the treatment of women with GDM, lack of data on the outcomes of importance for this review and the low-quality evidence based on two small studies, we cannot be certain if myo-inositol is useful as a treatment intervention for women with GDM. The available evidence is insufficient to support the use of myo-inositol. Further high-quality trials with large sample sizes are required to investigate the role of myo-inositol as a treatment or a co-treatment for women with gestational diabetes.

Brown J, Grzeskowiak L, Williamson K, Downie MR,Crowther CA. Insulin for the treatment of women with gestational diabetes. Cochrane Database of Systematic Reviews 2017;11): - Background Gestational diabetes mellitus (GDM) is associated with short- and long-term complications for the mother and her infant. Women who are unable to maintain their blood glucose concentration within pre-specified treatment targets with diet and lifestyle interventions will require anti-diabetic pharmacological therapies. This review explores the safety and effectiveness of insulin compared with oral anti-diabetic pharmacological therapies, non-pharmacological interventions and insulin regimens. Objectives To evaluate the effects of insulin in treating women with gestational diabetes. Search methods We searched Pregnancy and Childbirth’s Trials Register (1 May 2017), ClinicalTrials.gov , WHO International Clinical Trials Registry Platform (ICTRP ) (1 May 2017) and reference lists of retrieved studies. Selection criteria We included randomised controlled trials (including those published in abstract form) comparing: a) insulin with an oral anti-diabetic pharmacological therapy; b) with a non-pharmacological intervention; c) different insulin analogues; d) different insulin regimens for treating women with diagnosed with GDM. We excluded quasi-randomised and trials including women with pre-existing type 1 or type 2 diabetes. Cross-over trials were not eligible for inclusion. Data collection and analysis Two review authors independently assessed study eligibility, risk of bias, and extracted data. Data were checked for accuracy. Main results We included 53 relevant studies (103 publications), reporting data for 7381 women. Forty-six of these studies reported data for 6435 infants but our analyses were based on fewer number of studies/participants. Overall, the risk of bias was unclear; 40 of the 53 included trials were not blinded. Overall, the quality of the evidence ranged from moderate to very low quality . The primary reasons for downgrading evidence were imprecision, risk of bias and inconsistency. We report the results for our maternal and infant GRADE outcomes for the main comparison. Insulin versus oral anti-diabetic pharmacological therapy For the mother, insulin was associated with an increased risk for hypertensive disorders of pregnancy (not defined) compared to oral anti-diabetic pharmacological therapy (risk ratio (RR) 1.89, 95% confidence interval (CI) 1.14 to 3.12; four studies, 1214 women; moderate-quality evidence). There was no clear evidence of a difference between those who had been treated with insulin and those who had been treated with an oral anti-diabetic pharmacological therapy for the risk of pre-eclampsia (RR 1.14, 95% CI 0.86 to 1.52; 10 studies, 2060 women; moderate-quality evidence ); the risk of birth by caesarean section (RR 1.03, 95% CI 0.93 to 1.14; 17 studies, 1988 women;
moderate-quality evidence); or the risk of developing type 2 diabetes (metformin only) (RR 1.39, 95% CI 0.80 to 2.44; two studies, 754 women; moderate-quality evidence). The risk of undergoing induction of labour for those treated with insulin compared with oral anti-diabetic pharmacological therapy may possibly be increased, although the evidence was not clear (average RR 1.30, 95% CI 0.96 to 1.75; three studies, 348 women; I² = 32%; moderate-quality of evidence). There was no clear evidence of difference in postnatal weight retention between women treated with insulin and those treated with oral anti-diabetic pharmacological therapy (metformin) at six to eight weeks postpartum (MD -1.60 kg, 95% CI -6.34 to 3.14; one study, 167 women; low-quality evidence) or one year postpartum (MD -3.70, 95% CI -8.50 to 1.10; one study, 176 women; low-quality evidence). The outcomes of perineal trauma/tearing or postnatal depression were not reported in the included studies. For the infant, there was no evidence of a clear difference between those whose mothers had been treated with insulin and those treated with oral anti-diabetic pharmacological therapies for the risk of being born large-for-gestational age (average RR 1.01, 95% CI 0.76 to 1.35; 13 studies, 2352 infants; moderate-quality evidence); the risk of perinatal (fetal and neonatal death) mortality (RR 0.85; 95% CI 0.29 to 2.49; 10 studies, 1463 infants; low-quality evidence); for the risk of death or serious morbidity composite (RR 1.03, 95% CI 0.84 to 1.26; two studies, 760 infants; moderate-quality evidence); the risk of neonatal hypoglycaemia (average RR 1.14, 95% CI 0.85 to 1.52; 24 studies, 3892 infants; low-quality evidence); neonatal adiposity at birth (% fat mass) (mean difference (MD) 1.6%, 95% CI -3.77 to 0.57; one study, 82 infants; moderate-quality evidence); neonatal adiposity at birth (skinfold sum/mm) (MD 0.8 mm, 95% CI -2.33 to 0.73; random-effects; one study, 82 infants; very low-quality evidence); or childhood adiposity (total percentage fat mass) (MD 0.5%; 95% CI -0.49 to 1.49; one study, 318 children; low-quality evidence). Low-quality evidence also found no clear differences between groups for rates of neurosensory disabilities in later childhood: hearing impairment (RR 0.31, 95% CI 0.01 to 7.49; one study, 93 children), visual impairment (RR 0.31, 95% CI 0.03 to 2.90; one study, 93 children), or any mild developmental delay (RR 1.07, 95% CI 0.33 to 3.44; one study, 93 children). Later infant mortality, and childhood diabetes were not reported as outcomes in the included studies. We also looked at comparisons for regular human insulin versus other insulin analogues, insulin versus diet/standard care, insulin versus exercise and comparisons of insulin regimens, however there was insufficient evidence to determine any differences for many of the key health outcomes. Please refer to the main results for more information about these comparisons. Authors’ conclusions The main comparison in this review is insulin versus oral anti-diabetic pharmacological therapies. Insulin and oral anti-diabetic pharmacological therapies have similar effects on key health outcomes. The quality of the evidence ranged from very low to moderate, with downgrading decisions due to imprecision, risk of bias and inconsistency. For the other comparisons of this review (insulin compared with non-pharmacological interventions, different insulin analogues or different insulin regimens), there is insufficient volume of high-quality evidence to determine differences for key health outcomes. Long-term maternal and neonatal outcomes were poorly reported for all comparisons. The evidence suggests that there are minimal harms associated with the effects of treatment with either insulin or oral anti-diabetic pharmacological therapies. The choice to use one or the other may be down to physician or maternal preference, availability or severity of GDM. Further research is needed to explore optimal insulin regimens. Further research could aim to report data for standardised GDM outcomes. Plain language summary Insulin for the treatment of women with gestational diabetes What is the issue? The aim of this Cochrane review was to find out the effectiveness and safety of insulin compared with oral medication or non-pharmacological interventions for the treatment of gestational diabetes mellitus (GDM, which is diabetes diagnosed in pregnancy). It also looked at different timings for taking insulin during the day. We collected all the relevant studies (May 2017) and analysed the data. Why is this important? GDM can lead to both short- and long-term complications for the mother and her baby. Usually, diet and lifestyle advice is the first step, and women whose blood glucose remains too high may be treated with insulin, which is normally injected every day. Finding out if other treatment options are as safe and effective as insulin, is important, as these other treatments may be preferred by women who do not want to inject themselves with insulin. What evidence did we find? We searched for evidence on 1 May 2017 and found 53 studies reporting data for 7381 mothers and 46 studies reported data for 6435 babies. Overall, the quality of the evidence ranged from very low to moderate. Studies were undertaken in a variety of countries, including low-, middle- and high-income countries. Three studies reported that financial support or drugs had been provided by a pharmaceutical company and 36 studies did not provide any statement about the source of funding. For mothers with GDM, insulin was associated with an increased likelihood of hypertensive disorders of pregnancy (high blood pressure - not defined) although there was no evidence of any difference in pre eclampsia (high blood pressure, swelling and protein in the urine), birth by caesarean section, developing type 2 diabetes, or postnatal weight when women who had been treated with insulin were compared with women who had been treated with oral anti-diabetic medication. Insulin appeared to possibly increase the likelihood of induction of labour, when compared with oral anti-diabetic medication but these results are unclear. Damage to the perineum, return to pre-pregnancy weight or postnatal depression were not reported by the included studies.
For the baby, there was no evidence of a clear difference between groups in the risk of being born large-for-gestational age, death or serious illness after birth, low blood sugar, being overweight as a baby or as a child, having a hearing or visual impairment, or mild developmental delay at 18 months. None of the included studies looked at the baby’s health in childhood. We also looked at comparisons for regular human insulin versus other insulin types, insulin versus dietary advice with standard care, insulin versus exercise, and we also looked at comparisons of different insulin dosages and frequency. However, there was not enough evidence for us to be certain of any differences for many of the key health outcomes. What does this mean? The available evidence suggests that there are very few differences in short-term outcomes for the mother and baby between treatment with injected insulin and treatment with oral medication. There is not enough evidence yet for the long-term outcomes. Decisions about which treatment to use could be based on discussions between the doctor and the mother. Further research is needed to explore optimal insulin regimens for women with GDM. Future studies could aim to report long-term as well short-term outcomes for mothers and their babies.

Brown J, Martis R, Hughes B, Rowan J, Crowther CA. Oral anti-diabetic pharmacological therapies for the treatment of women with gestational diabetes. Cochrane Database of Systematic Reviews 2017;1: - Background Gestational diabetes mellitus (GDM) is a major public health issue with rates increasing globally. Gestational diabetes, glucose intolerance first recognised during pregnancy, usually resolves after birth and is associated with short- and long-term complications for the mother and her infant. Treatment options can include oral anti-diabetic pharmacological therapies. Objectives To evaluate the effects of oral anti-diabetic pharmacological therapies for treating women with GDM. Search methods We searched Cochrane Pregnancy and Childbirth’s Trials Register (14 May 2016), ClinicalTrials.gov, WHO ICTRP (14 May 2016) and reference lists of retrieved studies. Selection criteria We included published and unpublished randomised controlled trials assessing the effects of oral anti-diabetic pharmacological therapies for treating pregnant women with GDM. We included studies comparing oral anti-diabetic pharmacological therapies with 1) placebo/standard care, 2) another oral anti-diabetic pharmacological therapy, 3) combined oral anti-diabetic pharmacological therapies. Trials using insulin as the comparator were excluded as they are the subject of a separate Cochrane systematic review. Women with pre-existing type 1 or type 2 diabetes were excluded. Data collection and analysis Two review authors independently assessed trials for inclusion and trial quality. Two review authors independently extracted data and data were checked for accuracy. Main results We included 11 studies (19 publications) (1487 women and their babies). Eight studies had data that could be included in meta-analyses. Studies were conducted in Brazil, India, Israel, UK, South Africa and USA. The studies varied in diagnostic criteria and treatment targets for glycaemic control for GDM. The overall risk of bias was ‘unclear’ due to inadequate reporting of methodology. Using GRADE the quality of the evidence ranged from moderate to very low quality. Evidence was downgraded for risk of bias (reporting bias, lack of blinding), inconsistency, indirectness, imprecision and for oral anti-diabetic therapy versus placebo for generalisability. Oral anti-diabetic pharmacological therapies versus placebo/standard care There was no evidence of a difference between glibenclamide and placebo groups for hypertensive disorders of pregnancy (risk ratio (RR) 1.24, 95% confidence interval (CI) 0.81 to 1.90; one study, 375 women, very low-quality evidence), birth by caesarean section (RR 1.03, 95% CI 0.79 to 1.34; one study, 375 women, very low-quality evidence), perineal trauma (RR 0.98, 95% CI 0.06 to 15.62; one study, 375 women, very low-quality evidence) or induction of labour (RR 1.18, 95% CI 0.79 to 1.76; one study, 375 women; very low-quality evidence). No data were reported for development of type 2 diabetes or other pre-specified GRADE maternal outcomes (return to pre-pregnancy weight, postnatal depression). For the infant, there was no evidence of a difference in the risk of being born large-for-gestational age (LGA) between infants whose mothers had been treated with glibenclamide and those in the placebo group (RR 0.89, 95% CI 0.51 to 1.58; one study, 375, low-quality evidence). No data were reported for other infant primary or GRADE outcomes (perinatal mortality, death or serious morbidity composite, neurosensory disability in later childhood, neonatal hypoglycaemia, adiposity, diabetes). Metformin versus glibenclamide There was no evidence of a difference between metformin- and glibenclamide-treated groups for the risk of hypertensive disorders of pregnancy (RR 0.70, 95% CI 0.38 to 1.30; three studies, 508 women, moderate-quality evidence), birth by caesarean section (average RR 1.20, 95% CI 1.20; 95% CI 0.83 to 1.72, four studies, 554 women, I 2 = 61%, Tau 2 = 0.07 low-quality evidence), induction of labour (0.81, 95% CI 0.61 to 1.07; one study, 159 women; low-quality evidence) or perineal trauma (RR 1.67, 95% CI 0.22 to 12.5; two studies, 158 women; low-quality evidence). No data were reported for development of type 2 diabetes or other pre-specified GRADE maternal outcomes (return to pre-pregnancy weight, postnatal depression). For the infant there was no evidence of a difference between the metformin- and glibenclamide-exposed groups for the risk of being born LGA (average RR 0.67, 95% CI 0.24 to 1.83; two studies, 246 infants, I 2 = 54%; Tau 2 = 0.30 low-quality evidence). Metformin was associated with a decrease in a death or serious morbidity composite (RR 0.54, 95% CI 0.31 to 0.94; one study, 159 infants, low-quality evidence). There was no clear difference between groups for neonatal
hypoglycaemia (RR 0.86, 95% CI 0.42 to 1.77; four studies, 554 infants, low-quality evidence) or perinatal mortality (RR 0.92, 95% CI 0.06 to 14.55, two studies, 359 infants). No data were reported for neurosensory disability in later childhood or for adiposity or diabetes. Glibenclamide versus acarbose There was no evidence of a difference between glibenclamide and acarbose from one study (43 women) for any of their maternal or infant primary outcomes (caesarean section, RR 0.95, 95% CI 0.53 to 1.70; low-quality evidence; perinatal mortality - no events; low-quality evidence; LGA, RR 2.38, 95% CI 0.54 to 10.46; low-quality evidence). There was no evidence of a difference between glibenclamide and acarbose for neonatal hypoglycaemia (RR 6.33, 95% CI 0.87 to 46.32; low-quality evidence). There were no data reported for other pre-specified GRADE or primary maternal outcomes (hypertensive disorders of pregnancy, development of type 2 diabetes, perineal trauma, return to pre-pregnancy weight, postnatal depression, induction of labour) or neonatal outcomes (death or serious morbidity composite, adiposity or diabetes). Authors’ conclusions There were insufficient data comparing oral anti-diabetic pharmacological therapies with placebo/standard care (lifestyle advice) to inform clinical practice. There was insufficient high-quality evidence to be able to draw any meaningful conclusions as to the benefits of one oral anti-diabetic pharmacological therapy over another due to limited reporting of data for the primary and secondary outcomes in this review. Short- and long-term clinical outcomes for this review were inadequately reported or not reported. Current choice of oral anti-diabetic pharmacological therapy appears to be based on clinical preference, availability and national clinical practice guidelines. The benefits and potential harms of one oral anti-diabetic pharmacological therapy compared with another, or compared with placebo/standard care remains unclear and requires further research. Future trials should attempt to report on the core outcomes suggested in this review, in particular long-term outcomes for the woman and the infant that have been poorly reported to date, women’s experiences and cost benefit. Plain language summary Oral medication for the treatment of women with gestational diabetes What is the issue? Globally the number of women being diagnosed with gestational diabetes mellitus (GDM) is increasing. GDM is an intolerance to glucose leading to high blood sugars, first recognised during pregnancy and usually resolving after birth. Standard care involves lifestyle advice on diet and exercise. Treatment for some women includes oral anti-diabetic medications, such as metformin and glibenclamide, which are an alternative to, or can be used alongside, insulin to control the blood sugar. This review aimed to investigate benefits of taking oral medication to treat GDM in pregnant women. Another Cochrane Review compares the effects of insulin with oral anti-diabetic pharmacological therapies (Brown 2016). Why is this important? Women diagnosed with GDM are at a greater risk of experiencing complications such as high blood pressure during pregnancy and at birth. They have an increased risk of developing diabetes later in life. The babies of women who have been diagnosed with GDM can be larger than normal and this can cause injuries to the mother and the baby at birth. The birth is more likely to be induced or the baby born by caesarean section. These babies are at risk of developing diabetes as children or young adults. Finding the best medications to treat the women and prevent the complications that are linked to GDM is therefore important. What evidence did we find? We searched for studies on 14 May 2016. We included 11 randomised controlled trials involving 1487 mothers and their babies (but only eight trials contributed data to our analyses). The evidence was limited by the quality and number of studies and we advise caution when looking at the results. The criteria for diagnosis of GDM and treatment targets varied between studies, and each outcome is based on few studies with low numbers of women. Three studies compared oral medication with placebo/standard care but the following findings are from a single study (375 women). The quality of the evidence was very low or low. We found no differences between the oral medication and placebo group for the risk of high blood pressure, birth by caesarean section, induction of labour or perineal trauma. The number of babies born large-for-gestational age, with low blood sugars or dying at birth was not clearly different between the groups. Two studies (434 women) reported no difference in the need for insulin between the oral medication and placebo group. Six studies compared metformin with glibenclamide. The quality of the evidence was very low to moderate. We found no difference between metformin and glibenclamide for the risk of high blood pressure (three studies, 508 women, moderate-quality evidence), birth by caesarean section (four studies, 554 women, low-quality evidence), perineal trauma (two studies, 308 women, low-quality evidence) or induction of labour (one study, 159 women, low-quality evidence). We found no difference between metformin and glibenclamide for the baby having low blood sugars (four studies, 554 infants, low-quality evidence), being born large-for-gestational age (two studies, 246 infants) or dying at birth (all low- or very low-quality evidence). In one study, the babies of the mothers taking metformin were at reduced risk of having any serious outcome (low blood sugar, jaundice, being born large, breathing problems, injury at birth or death combined) (low-quality evidence). One small study (43 women) comparing glibenclamide with acarbose reported no differences in outcomes for mothers or their babies. None of the included studies provided any data on many of the outcomes pre-specified in this review, including long-term outcomes for the mother or for the baby as a child or an adult. What does this mean? There is not enough high-quality evidence available to guide us on if oral medication has better outcomes for women with gestational diabetes, and their babies, compared with a placebo or if one oral medication has better health
Objectives To assess if antenatal dietary supplementation with myo-inositol is safe and effective, for the mother and fetus, in preventing gestational diabetes. Search methods We searched the Pregnancy and Childbirth Group’s Trials Register, ClinicalTrials.gov, WHO ICTRP (2 November 2015) and reference lists of retrieved studies. Selection criteria We sought published and unpublished randomised controlled trials, including conference abstracts, assessing the effects of myo-inositol for the prevention of gestational diabetes mellitus (GDM). Quasi-randomised and cross-over trials were not eligible for inclusion, but cluster designs were eligible. Participants in the trials were pregnant women. Women with pre-existing type 1 or type 2 diabetes were excluded. Trials that compared the administration of any dose of myo-inositol, alone or in a combination preparation were eligible for inclusion. Trials that used no treatment, placebo or another intervention as the comparator were eligible for inclusion. Data collection and analysis Two review authors independently assessed trials for inclusion, risk of bias and extracted the data. Data were checked for accuracy. Main results We included four randomised controlled trials (all conducted in Italy) reporting on 567 women who were less than 11 weeks’ to 24 weeks’ pregnant at the start of the trials. The trials had small sample sizes and one trial only reported an interim analysis. Two trials were open-label. The overall risk of bias was unclear. For the mother, supplementation with myo-inositol was associated with a reduction in the incidence of gestational diabetes compared with control (risk ratio (RR) 0.43, 95% confidence interval (CI) 0.29 to 0.64; three trials; n = 502 women). Using GRADE methods this evidence was assessed as low with downgrading due to unclear risk of bias for allocation concealment in two of the included trials and lack of generalisability of findings. For women who received myo-inositol supplementation, the incidence of GDM ranged from 8% to 18%; for women in the control group, the incidence of GDM was 28%, using International Association of Diabetes and Pregnancy Study Groups Consensus Panel 2010 criteria to diagnose GDM. Two trials reported on hypertensive disorders of pregnancy, a primary maternal outcome of this review. There was no clear difference in risk of hypertensive disorders of pregnancy between the myo-inositol and control groups (average RR 0.43, 95% CI 0.02 to 8.41; two trials; n = 398 women; Tau 2 = 3.23; I 2 = 69%). Using GRADE methods, this evidence was assessed as very low, with downgrading due to wide confidence intervals with very low event rates, a small sample size, and lack of binding and unclear allocation concealment methods, and a lack of generalisability. For women who received myo-inositol the risk of hypertensive disorders of pregnancy ranged from 0% to 33%; for women in the control group the risk was 4%. For the infant, none of the included trials reported on the primary neonatal outcomes of this systematic review (large-for-gestational age, perinatal mortality, mortality or morbidity composite). In terms of this review’s secondary outcomes, there was no clear difference in the risk of caesarean section between the myo-inositol and control groups (RR 0.95, 95% CI 0.76 to 1.19; two trials; n = 398 women). Using GRADE methods, this evidence was assessed as low, with downgrading due to unclear risk of bias in one trial and lack of generalisability. For women who received myo-inositol supplementation, the risk of having a caesarean section ranged from 34% to 54%; for women in the control group the was 45%. There were no maternal adverse effects of therapy in the two trials that reported on this outcome (the other two trials did not report this outcome). Two trials found no clear difference in the risk of macrosomia between infants whose mothers received myo-inositol supplementation compared with controls (average RR 0.35, 95% CI 0.02 to 6.37; two trials; n = 398 infants; Tau 2 = 3.33; I 2 = 73%). Similarly, there was no clear difference between groups in terms of neonatal hypoglycaemia (RR 0.36, 95% CI 0.01 to 8.66) or shoulder dystocia (average RR 2.33, 95% CI 0.12 to 44.30, Tau 2 = 3.24; I 2 = 72%). There was a lack of data available for a large number of maternal and neonatal secondary outcomes, and no data for any of the long-term childhood or adulthood outcomes, or for health service cost outcomes. Authors’ conclusions Evidence from four trials of antenatal dietary supplementation with myo-inositol during pregnancy shows a potential benefit for reducing the incidence of gestational diabetes. No data were reported for any of this review’s primary neonatal outcomes. There were very little outcome data for the majority of this review’s secondary outcomes. There is no clear evidence of a difference for macrosomia when compared with control. The current evidence is based on small trials that are not
powered to detect differences in outcomes including perinatal mortality and serious infant morbidity. All of the included studies were conducted in Italy which raises concerns about the lack of generalisability of the evidence to other settings. There is evidence of inconsistency and indirectness and as a result, many of the judgements on the quality of the evidence were downgraded to low or very low quality (GRADEpro Guideline Development Tool). Further trials for this promising antenatal intervention for preventing gestational diabetes are encouraged and should include pregnant women of different ethnicities and varying risk factors and use of myo-inositol (different doses, frequency and timing of administration) in comparison with placebo, diet and exercise or pharmacological interventions. Outcomes should include potential harms including adverse effects. Plain language summary Taking myo-inositol as a dietary supplement during pregnancy to prevent the development of gestational diabetes What is the issue? This review aimed to investigate if myo-inositol is an effective antenatal dietary supplement for preventing gestational diabetes in pregnant women. Women who develop gestational diabetes have a higher risk of experiencing complications during pregnancy and birth, as well as developing diabetes later on in life. The babies of mothers who have gestational diabetes can be larger than they should be potentially causing injuries to the babies at birth. These babies are at risk of diabetes even as young children or young adults. Why is this important? The number of women being diagnosed with gestational diabetes is increasing around the world so finding simple and cost-effective ways to prevent women developing gestational diabetes is important. Myo-inositol is a naturally occurring sugar found in cereals, corn, green vegetables and meat that has a role in the body’s sensitivity to insulin. What evidence did we find? We searched for studies on 2 November 2015 and included four small randomised controlled trials involving a total of 567 women who were less than 11 weeks’ to 24 weeks’ pregnant at the start of the trials. The quality of the evidence was assessed as low or very low and the overall risk of bias was unclear. Myo-inositol was associated with a reduction in the rate of gestational diabetes (1 w quality evidence), reducing the incidence from 28% in women who did not take the supplement, to between 8% and 18% in the women who took it. There was no difference between groups in terms of the number of women who had hypertensive disorders of pregnancy (including pre-eclampsia, eclampsia and abnormally high blood pressure during pregnancy) (very low quality evidence). The trials did not provide any information about the number of babies that died (either before being born or shortly afterwards) or babies that were large-for-gestational age. There were no maternal adverse effects of therapy in the two trials that reported on this outcome (the other two trials did not mention this). This review did not find any impact on other outcomes such as the risk of having a caesarean section (low quality evidence), a large baby, obstructed labour when the baby’s shoulder becomes stuck (shoulder dystocia) or a baby with low blood glucose levels. This may be due to the trials being too small to detect differences in these outcomes and the outcomes not being reported by all trials. All four trials were from Italy. The included trials did not report on a large number of other mother and baby outcomes listed in this review and nor were there any data relating to longer-term outcomes for the mother or the infant, or the cost of health services. What does this mean? Myo-inositol as a dietary supplement during pregnancy shows promise in preventing gestational diabetes but there is not enough evidence at this stage to support its routine use. Further large, well-designed, randomised controlled trials are required to assess the effectiveness of myo-inositol in preventing gestational diabetes and improving other health outcomes for mothers and their babies. Ideally, future studies should consider involving women from different ethnicities and with differing risk factors for gestational diabetes. It would be useful for future studies to consider the ways that myo-inositol can be used (different doses, frequency and when to take it) and compare the intervention with a placebo control, diet and exercise or pharmacological interventions. We recommend that future studies utilise the outcomes listed in this review and that potential harms, including adverse effects are included.

Culliney KAT, Parry GK, Brown J, Crowther CA. Regimens of fetal surveillance of suspected large-for-gestational-age fetuses for improving health outcomes. Cochrane Database of Systematic Reviews 2016;4:
- Background Policies and protocols vary widely for fetal surveillance in a pregnancy where the fetus is suspected to be large-for-gestational-age (LGA). All ultimately culminate in decisions about the mode and timing of birth. LGA is known to be associated with increased risks to both the mother and baby. Interventions based on surveillance regimen findings may be associated with risks to the mother and baby. Objectives To assess the effectiveness or efficacy of different antenatal surveillance methods for the suspected LGA fetus on important health outcomes for the mother and baby. Search methods We searched the Cochrane Pregnancy and Childbirth Group’s Trials Register (30 August 2015), ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) (21 August 2015). Selection criteria Published and unpublished randomised, quasi-randomised and cluster-randomised trials comparing the effects of described antenatal fetal surveillance regimens for women with suspected LGA infants. Data collection and analysis We identified no studies that met the inclusion criteria for this review. Main results There are no included trials. Authors’ conclusions We found no randomised controlled trials that assessed the effect of antenatal fetal surveillance regimens of a suspected LGA fetus on important health outcomes for the mother and baby.
There has been a rise in the prevalence of LGA babies over the past few decades in many countries. Research is therefore required on regimens of antenatal surveillance of suspected LGA infants, in order to guide practice and improve the health outcomes for the mother and infant. In particular, randomised control trials to investigate whether serial antenatal clinic and ultrasound assessments of suspected LGA infants (including liquor volume and markers of fetal adiposity) would be useful, to assess whether surveillance methods improve health outcomes. In addition, as there are concerns that identifying suspected LGA fetuses may lead to unnecessary maternal anxiety, investigations and interventions, any such trial would need to assess the risks as well as benefits of regimens of fetal surveillance for suspected LGA fetuses. Plain language summary Use of different methods of detecting if a baby is large-for-gestational-age, to improve health outcomes What is the issue? A baby may sometimes grow to be bigger than expected and be born with a high birthweight. When overgrowth of the baby is suspected during a pregnancy the mother can have extra scheduled antenatal visits and tests to assess her health and the health of her developing baby. Why is this important? Tests can detect if there are signs of any deterioration in the baby's condition, or development of complications in the mother. The specified frequency and combinations of tests vary with local protocols and policies. Tests may include fetal movement counting, fetal heart rate assessment (cardiotocography), checking the mother's blood sugars or the use of ultrasound for fetal growth scans, Doppler ultrasound examination of fetal blood vessels and assessing the volume of fluid around the baby. Large babies are associated with increased risks to both the mother and baby, including increased risk of intra-uterine death and stillbirth. At birth the baby is at a higher risk of low oxygen levels, shoulder dystocia, nerve injuries, bone fracture, low blood sugar levels, and admission to the neonatal intensive care unit. Maternal complications include prolonged labour, operative births including caesarean section, perineal trauma, postpartum haemorrhage and uterine rupture. Interventions that may slow growth acceleration and improve health outcomes for the mother and her baby include dietary advice, lifestyle modification, and in women with diabetes or gestational diabetes blood glucose monitoring and insulin therapy. What evidence did we find? We searched for studies on 10 August 2015 but did not find any randomised controlled trials looking at the effects of performing extra tests on health outcomes in pregnant women with overgrowth of the baby after 20 weeks gestation. What does this mean? There is a need for randomised controlled trials in this area in order to inform clinical practice when large babies are identified during a pregnancy, to assess if extra tests or surveillance can improve the health of these women and their babies. It is also important to identify any harms associated with extra tests and surveillance, as identifying women with suspected large babies may lead to unnecessary maternal anxiety with additional investigations and interventions, including induction of labour or caesarean section.

Dodd JM, Grivell RM, Deussen AR, Hague WM. Metformin for women who are overweight or obese during pregnancy for improving maternal and infant outcomes. Cochrane Database of Systematic Reviews 2018;7(CD010564

BACKGROUND: There has been considerable interest in providing antenatal dietary and lifestyle advice for women with obesity or who are overweight during pregnancy, as a strategy to limit gestational weight gain and improve maternal and infant health. However, such antenatal interventions appear to have a modest effect on gestational weight gain and other clinical pregnancy and birth outcomes and additional strategies are required. Metformin is an oral insulin-sensitising medication that acts to decrease blood glucose concentrations. Metformin is commonly used in the treatment of type 2 diabetes mellitus and polycystic ovarian syndrome, and is being used increasingly in the treatment of gestational diabetes, having been shown to result in decreased rates of caesarean birth and neonatal hypoglycaemia. Metformin may be an adjuvant therapy to current antenatal strategies in pregnant women with obesity or who are overweight, acting to reduce glucose production in the liver and improve glucose uptake in smooth muscle cells, and therefore improve the overall metabolic health of women in pregnancy and reduce the risk of known adverse pregnancy outcomes.

OBJECTIVES: To evaluate the role of metformin in pregnant women with obesity or who are overweight, on maternal and infant outcomes, including adverse effects of treatment and costs.

SEARCH METHODS: We searched Cochrane Pregnancy and Childbirth's Trials Register, ClinicalTrials.gov, the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (11 October 2017), and reference lists of retrieved studies.

SELECTION CRITERIA: All published and unpublished randomised controlled trials evaluating metformin use (compared with placebo or no metformin) in women with obesity or who are overweight in pregnancy for improving outcomes, alone or in combination with other interventions were eligible for inclusion.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. We used the GRADE approach to assess the quality of the evidence.
MAIN RESULTS: We included three studies which randomised women (1099) with a body mass index (BMI) of 30 kg/m² (1 study) and 35 kg/m² (2 studies), with outcomes available for 1034 participants. None of the studies assessed women with a BMI between 25 kg/m² and 29.9 kg/m², therefore we could not assess the use of metformin in women considered overweight. We did not identify studies of metformin in combination with another treatment. Two other studies are ongoing. All three included studies were randomised controlled trials and compared metformin with placebo, commencing early in the second trimester. Doses ranged from 500 mg twice daily to 3.0 g per day. All three studies (two in the UK, one in Egypt) included women attending hospitals for antenatal care. Two studies were generally at a low risk of bias across the majority of domains. We assessed the third study as being at an unclear risk of selection bias, performance and detection bias due to insufficient information in the report. We assessed the trial as being at a low risk of attrition bias and other bias; we felt it was at a high risk of reporting bias. The primary outcome for this review was infant birthweight large-for-gestational-age (> 90th centile for gestational age and infant sex). Women who received metformin or placebo had a similar risk of their baby being born large for his or her gestational age (risk ratio (RR) 0.95, 95% confidence interval (CI) 0.70 to 1.30; 2 studies, 831 infants; high-quality evidence). Women who received metformin may have a slightly lower gestational weight gain (mean difference (MD) -2.60 kg, 95% CI -5.29 to 0.10; 3 studies, 899 women; low-quality evidence). Metformin may make little or no difference in the risk of women developing gestational hypertension (average RR 1.02, 95% CI 0.54 to 1.94; 3 studies, 1040 women; low-quality evidence) or pre-eclampsia (RR 0.74, 95% CI 0.09 to 6.28; 2 studies, 840 women; low-quality evidence). Metformin probably makes little or no difference in the risk of women developing gestational diabetes (RR 0.85, 95% CI 0.61 to 1.19; 3 studies, 892 women; moderate-quality evidence). One study of 400 women reported women receiving metformin were more likely to experience any adverse effect compared with women receiving placebo (RR 1.63, 95% CI 1.27 to 2.08; 1 study, 400 women). Adverse effects included abdominal pain, diarrhoea, or headache. When considering individual side effects, women receiving metformin were more likely to experience diarrhoea than women receiving placebo (RR 2.34, 95% CI 1.74 to 3.14; 797 women; 2 studies, 797 women; high-quality evidence). No other important differences were identified between Metformin and placebo for other maternal secondary outcomes, including: caesarean birth, birth before 37 weeks of pregnancy, shoulder dystocia, perineal tear, or postpartum haemorrhage. In terms of other infant outcomes, there was little or no difference in the infant birthweight (MD 0.39 g, 95% CI -81.15 to 93.92; 2 studies, 834 infants; high-quality evidence). There were no other important differences identified for other infant secondary outcomes in this review: hypoglycaemia (low blood sugar); hyperbilirubinaemia (jaundice); Apgar score less than 7 at five minutes; or stillbirth and neonatal death. Only one study reported admission to the neonatal intensive care unit (NICU), indicating similar rates of admission between women receiving metformin or placebo; no other admission data were reported to assess differences in costs.

AUTHORS' CONCLUSIONS: There is insufficient evidence to support the use of metformin for women with obesity in pregnancy for improving maternal and infant outcomes. Metformin was, however, associated with increased risk of adverse effects, particularly diarrhoea. The quality of the evidence in this review varied from high to low, with downgrading decisions based on study limitations and inconsistency. There were only a small number of studies included in this review. Furthermore, none of the included studies included women categorised as ‘overweight’ and no trials looked at metformin in combination with another treatment. Future research is required in order to further evaluate the role of metformin therapy in pregnant women with obesity or who are overweight, as a strategy to improve maternal and infant health, alone or as an adjuvant to dietary and lifestyle advice.

Farrar D, Duley L, Dowswell T, Lawlor DA. Different strategies for diagnosing gestational diabetes mellitus to improve maternal and infant health. Cochrane Database of Systematic Reviews 2017;8:
- Background Gestational diabetes mellitus (GDM) is carbohydrate intolerance resulting in hyperglycaemia with onset or first recognition during pregnancy. If untreated, perinatal morbidity and mortality may be increased. Accurate diagnosis allows appropriate treatment. Use of different tests and different criteria will influence which women are diagnosed with GDM. This is an update of a review published in 2011 and 2015. Objectives To evaluate and compare different testing strategies for diagnosis of gestational diabetes mellitus to improve maternal and infant health while assessing their impact on healthcare service costs. Search methods We searched Cochrane Pregnancy and Childbirth’s Trials Register, ClinicalTrials.gov, WHO International Clinical Trials Registry Platform (ICTRP) (9 January 2017) and reference lists of retrieved studies. Selection criteria We included randomised trials if they evaluated tests carried out to diagnose GDM. We excluded studies that used a quasi-random model, cluster-randomised or cross-over trials. Data collection and analysis Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. The quality of the evidence was assessed using the GRADE approach. Main
results. We included a total of seven small trials, with 1420 women. One trial including 726 women was identified by this update and examined the two step versus one step approach. These trials were assessed as having varying risk of bias, with few outcomes reported. We prespecified six outcomes to be assessed for quality using the GRADE approach for one comparison: 75 g oral glucose tolerance test (OGTT) versus 100 g OGTT; data for only one outcome (diagnosis of gestational diabetes) were available for assessment. One trial compared three different methods of delivering glucose: a candy bar (39 women), a 50 g glucose polymer drink (40 women) and a 50 g glucose monomer drink (43 women). We have included the results reported by this trial as separate comparisons. No trial reported on measures of costs of health services. We examined six main comparisons. 75 g OGTT versus 100 g OGTT (1 trial, 248 women): women who received 75 g OGTT had a higher relative risk of being diagnosed with GDM (risk ratio (RR) 2.55, 95% confidence interval (CI) 0.96 to 6.75; very-low quality evidence ). No data were reported for the following additional outcomes prespecified for GRADE assessment: caesarean section, macrosomia > 4.5 kg or however defined in the trial, long-term type 2 diabetes maternal, long-term type 2 diabetes infant and economic costs. Candy bar versus 50 g glucose monomer drink (1 trial, 60 women): more women receiving the candy bar, rather than glucose monomer, preferred the taste of the candy bar (RR 0.60, 95% CI 0.42 to 0.86) and 1-hour glucose was less with the candy bar. There were no differences in the other outcomes reported (maternal side effects). No infant outcomes were reported or any review primary outcomes. 50 g glucose polymer drink versus 50 g glucose monomer drink (3 trials, 239 women): mean difference (MD) in gestation at birth was -0.80 weeks (1 trial, 100 women; 95% CI -1.69 to 0.09). Total side effects were less common with the glucose polymer drink (1 trial, 63 women; RR 0.21, 95% CI 0.07 to 0.59), and no clear difference in taste acceptability was reported (1 trial, 63 women; RR 0.99, 95% CI 0.76 to 1.29). Fewer women reported nausea following the 50 g glucose polymer drink compared with the 50 g glucose monomer drink (1 trial, 66 women; RR 0.29, 95% CI 0.11 to 0.78). No other measures of maternal morbidity or outcomes for the infant were reported. 50 g glucose food versus 50 g glucose drink (1 trial, 30 women): women receiving glucose in their food, rather than as a drink, reported fewer side effects (RR 0.0 . 95% CI 0.01 to 0.56). No clear difference was noted in the number of women requiring further testing (RR 0.14, 95% CI 0.01 to 2.55). No other measures of maternal morbidity or outcome were reported for the infant or review primary outcomes. 75 g OGTT World Health Organization (WHO) criteria versus 75 g OGTT American Diabetes Association (ADA) criteria (1 trial, 116 women): no clear differences in included outcomes were observed between women who received the 75 g OGTT and were diagnosed using criteria based on WHO (1999) recommendations and women who received the 75 g OGTT and were diagnosed using criteria recommended by the ADA (1979). Outcomes measured included diagnosis of gestational diabetes (RR 1.47, 95% CI 0.66 to 3.25), caesarean section (RR 1.07, 95% CI 0.85 to 1.35), macrosomia defined as > 90th percentile by ultrasound or birthweight equal to or exceeding 4000 g (RR 0.73, 95% CI 0.19 to 2.79), stillbirth (RR 0.49, 95% CI 0.02 to 11.68) and instrumental birth (RR 0.21, 95% CI 0.01 to 3.94). No other secondary outcomes were reported. Two-step approach (50 g oral glucose challenge test followed by selective 100 g OGTT Carpenter and Coustan criteria) versus one-step approach (universal 75 g OGTT ADA criteria) (1 trial, 726 women): women allocated the two-step approach had a lower risk of being diagnosed with GDM at 11 to 14 weeks’ gestation compared to women allocated the one-step approach (RR 0.51, 95% CI 0.28 to 0.95). No other primary or secondary outcomes were reported. Authors’ conclusions There is insufficient evidence to suggest which strategy is best for diagnosing GDM. Large randomised trials are required to establish the best strategy for correctly identifying women with GDM. Plain language summary Different strategies for diagnosing gestational diabetes mellitus (GDM) to improve maternal and infant health What is the issue? We aimed to evaluate and compare different ways of diagnosing gestational diabetes mellitus (GDM). We searched for all relevant studies in January 2017. Why is this important? Between seven and 24 pregnant women in every 100 develop GDM. GDM is when there is an inability to process carbohydrates properly, which leads to high blood sugar (hyperglycaemia). GDM can result in increased risks of problems around the time of birth for the mother and her baby. Treatment can reduce these risks, and therefore diagnosing the condition accurately means that treatment can be given to improve the health of mothers and their babies. Different testing strategies aim to diagnose GDM. We wanted to compare the different strategies, to see how they affected the health of women and their infants, and to assess the cost of the strategies to the healthcare service. What evidence did we find? We found seven trials. A total of 1420 women were included, in settings in Turkey, Mexico, Nigeria, New Zealand, Canada and the USA. Across the trials, different testing approaches and criteria were evaluated as were different diagnostic tests including different oral glucose tolerance test loads; a glucose drink; a candy bar and food high in glucose. Women were given these items to eat/drink, and this was then followed by a blood test to measure blood sugar levels and questionnaires. In some tests, women were required to fast from the night before. The main outcomes we looked for were frequency of diagnosis, incidence of caesarean section, assisted birth and vaginal birth, and incidence of macrosomia in babies (larger than normal weight at birth). Other outcomes spanned a range, including any side effects of the tests, the mothers’ preferences, and the health of the babies. There were a number of weaknesses among the studies: the methodology was not clear and there were important gaps in
the data. The studies in this review do not provide enough evidence to guide clinical practice and health policy regarding identifying women with GDM. What does this mean? We are uncertain about which strategies to diagnose GDM are better, as we have assessed the quality of evidence as very low. Large randomised trials are needed to establish the best way for identifying women with GDM.

Farrar D, Tuffnell DJ, West J, West HM. Continuous subcutaneous insulin infusion versus multiple daily
injections of insulin for pregnant women with diabetes. Cochrane Database of Systematic Reviews 2016;6: - Background Diabetes results in a rise in blood glucose above normal physiological levels; if untreated this may cause damage to many systems including the cardiovascular and renal systems. Pregnancy increases resistance to insulin action; for those women who have pre-gestational diabetes, this results in an increasing insulin requirement. There are several methods of administering insulin. Conventionally, insulin has been administered subcutaneously, formally referred to as intensive conventional treatment, but now more usually referred to as multiple daily injections (MDI). An alternative method of insulin administration is the continuous subcutaneous insulin infusion pump (CSII). Objectives To compare CSII with MDI of insulin for pregnant women with pre-existing and gestational diabetes. Search methods We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 March 2016) and reference lists of retrieved studies. Selection criteria Randomised trials comparing CSII with MDI for pregnant women with diabetes. Data collection and analysis. Three review authors independently assessed studies and two review authors extracted data. Disagreements were resolved through discussion with the third author. We assessed the quality of the evidence using the GRADE approach. Main results. We included five single-centre trials (undertaken in Italy) with 153 women and 154 pregnancies in this review. There were no clear differences in the primary outcomes reported between CSII and MDI in the included trials: caesarean section (risk ratio (RR) 1.09, 95% confidence interval (CI) 0.66 to 1.77; three trials, 71 women, evidence graded very low), large-for-gestational age (RR 4.15, 95% CI 0.49 to 34.95; three trials, 73 infants; evidence graded very low), and perinatal mortality (RR 2.33, 95% CI 0.38 to 14.32; four trials, 83 infants, evidence graded very low). Other primary outcomes were not reported in these trials (hypertensive disorders of pregnancy, development of type 2 diabetes, composite outcome of serious neonatal outcomes, and neurosensory disability). There was no clear evidence of differences in the maternal secondary outcomes: maternal weight gain during pregnancy, 24 hour mean blood glucose in each trimester, mean maternal HbA1c in each trimester, maternal hypoglycaemia, and maternal hyperglycaemia. The included studies did not report several GRADE outcomes: perineal trauma, return to pre-pregnancy weight, postnatal depression, induction of labour. Many maternal secondary outcomes were also not reported. In two trials, including a total of 61 infants, CSII was associated with an increase in mean birthweight compared with MDI (mean difference (MD) 14.40 g, 95% CI 7.90 g to 20.90 g; P = 0.05). However, the large CI including anything from a small reduction to an increase in mean birthweight and the lack of a difference in macrosomia rate (RR 3.20, CI 0.14 to 72.62; two trials, 61 infants) suggests uncertainty. Large-for-gestational age (see above), and small-for-gestational age also suggests uncertainty of effect. No significant differences were found in: gestation at delivery, preterm birth < 37 weeks' gestation, preterm birth < 32 weeks' gestation, neonatal hyperglycaemia (evidence graded very low), respiratory distress syndrome, neonatal hyperbilirubinaemia, and fetal anomaly. There were no data reported on many important infant outcomes, including the GRADE outcomes adiposity and diabetes. There was no follow-up of infants in childhood or adulthood, so longer-term outcomes were not reported. The only outcome reported for use of health service resources was maternal days hospitalised, which did not show a difference between groups in the small number of women included (MD 9.40, CI -6.04 to 24.84; one trial, 10 women). The methods used by the trials were poorly reported, for example although blinding of participants and clinicians regarding intervention allocation is impossible, it is possible to blind assessors and this along with other aspects of trial methods was not reported, which means that the trials are at an unclear or high risk of bias. We do not know if the women who participated were representative, and therefore if the results can be generalised. Most GRADE outcomes were not reported. For the GRADE outcomes that were reported, our assessment was that the evidence is very low quality (caesarean section, large-for-gestational age, perinatal mortality, and neonatal hyperglycaemia). This was due to design limitations in the included trials, small sample sizes in the trials contributing data, wide CIs crossing both the line of no effect and the line of appreciable benefit and/or harm, and often few events. We are therefore uncertain whether CSII or MDI improves outcomes for pregnant women with diabetes and their infants, and the results of further studies may differ substantially from those presented in this review. Authors' conclusions There is no evidence to support the use of one particular form of insulin administration over another for pregnant women with diabetes. There are only a small number of trials appropriate for meta-analysis, a small number of women included and questionable generalisability of the trial population. Pump technology has progressed since these trials were undertaken. Well-designed randomised trials are required to evaluate comparisons such as patch pumps against MDI and more conventional CSII against MDI. These trials should be adequately powered to assess the effect of interventions, and report the core set of outcomes used in Cochrane reviews of diabetes in
pregnancy. Trials to assess the effects of pumps on birthweight and macrosomia rates are needed. It would be beneficial for future trials to undertake longer-term follow-up of participants and their infants, assess women’s preferences, and conduct an economic evaluation. Plain language summary Continuous subcutaneous insulin infusion versus multiple daily injections of insulin for pregnant women with diabetes What is the issue? Diabetes is a condition in which glucose (sugar) in the blood is too high because the body does not respond to insulin or not enough insulin is made. Insulin is a hormone made by the pancreas, which allows glucose to enter the cells where it is used as fuel by the body. Controlling blood sugar levels is important because levels that are too high or too low can affect the brain and other organs of the body. Poor blood sugar control in pregnant women with diabetes can lead to large babies who may then have a difficult birth. It also increases the chance of abnormalities in the baby, miscarriage, or stillbirth. Traditionally, insulin is given as multiple daily injections (MDI), however a small pump can continuously give insulin through a fine tube under the skin (CSII). Why is this important? An insulin pump may help pregnant women keep their blood glucose more stable than multiple injections. It might stop the woman’s blood sugar level going too high or too low, which would be better for the mother and her baby and it may be more acceptable to women. This review compared the positive and negative effects of CSII and MDI to work out which is best for mothers and infants. What evidence did we find? Five randomised trials involving 153 women (154 pregnancies) were included. These trials did not report many of the outcomes we had hoped to look at. The evidence was judged to be very low quality for important outcomes (caesarean section, large-for-gestational age, perinatal mortality, and neonatal hypoglycaemia). This was because the trials were small, may not have been fair tests, and did not show a clear difference between MDI and CSII. There were no clear differences in any of the reported outcomes between women who had insulin via a pump rather than as multiple injections. For mothers, this included caesarean section, weight gain during pregnancy, and blood sugar levels. For babies, this included the baby’s weight, if they were born premature, and problems such as difficulty breathing, a low Apgar score at birth, low blood sugar, jaundice, or physical abnormalities. In one small trial, there was no difference in the number of days mothers spent in hospital. This was the only measure of cost or use of health service resources reported. What does this mean? The trials did not provide enough information to know whether an insulin pump or multiple injections are better for a pregnant woman with diabetes or her baby. More research is needed, with bigger groups of women, good reporting of how the trials were undertaken, more outcomes assessed and reported, and using the latest pump technology and insulins.

Han S, Crowther CA, Middleton P. Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria. Cochrane Database of Systematic Reviews 2012;1:

- 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 macromomic 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 an 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.

Han S, Middleton P, Crowther CA. Exercise for pregnant women for preventing gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2012;7):

- Background Gestational diabetes mellitus (GDM) affects a significant number of women each year. GDM is associated with a wide range of adverse outcomes for women and their babies. Recent observational studies have found physical activity during normal pregnancy decreases insulin resistance and therefore might help to decrease the risk of developing GDM. Objectives To assess the effects of physical exercise for pregnant women for preventing glucose intolerance or GDM. Search methods We searched the Cochrane Pregnancy and Childbirth Group’s Trials Register (2 April 2012), ClinicalTrials.gov (2 April 2012) and the WOMBAT Perinatal Trials Registry (2 April 2012). Selection criteria Randomised and cluster-randomised trials assessing the effects of exercise for preventing pregnancy glucose intolerance or GDM. Data collection and analysis Two review authors independently assessed study eligibility, extracted data and assessed the risk of bias of included studies. Main results We included five trials with a total of 1115 women and their babies (922 women and their babies contributed outcome data). Four of the five included trials had small sample sizes with one large trial that recruited 855 women and babies. All five included trials had a moderate risk of bias. When comparing women receiving additional exercise interventions with those having routine antenatal care, there was no significant difference in GDM incidence (three trials, 826 women, risk ratio (RR) 1.10, 95% confidence interval (CI) 0.66 to 1.84), caesarean section (two trials, 934 women, RR 1.33, 95% CI 0.97 to 1.84) or operative vaginal birth (two trials, 934 women, RR 0.83, 95% CI 0.58 to 1.17). No trial reported the infant primary outcomes prespecified in the review. None of the five included trials found significant differences in insulin sensitivity. Evidence from one single large trial suggested no significant difference in the incidence of developing pregnancy hyperglycaemia not meeting GDM diagnostic criteria, pre-eclampsia or admission to neonatal ward between the two study groups. Babies born to women receiving exercise interventions had a non-significant trend to a lower ponderal index (mean difference (MD) -0.08 gram x 100 m 3 , 95% CI -0.18 to 0.02, one trial, 84 infants). No significant differences were seen between the two study groups for the outcomes of birthweight (two trials, 167 infants, MD -102.87 grams, 95% CI -235.34 to 29.60), macrosomia (two trials, 934 infants, RR 0.91, 95% CI 0.68 to 1.22), or small-for-gestational age (one trial, 84 infants, RR 1.05, 95% CI 0.25 to 4.40) or gestational age at birth (two trials, 167 infants, MD -0.04 weeks, 95% CI -0.37 to 0.29) or Apgar score less than seven at five minutes (two trials, 919 infants, RR 1.00, 95% CI 0.27 to 3.65). None of the trials reported long-term outcomes for women and their babies. No information was available on health services costs. Authors’ conclusions There is limited randomised controlled trial evidence available on the effect of exercise during pregnancy for preventing pregnancy glucose intolerance or GDM. Results from three randomised trials with moderate risk of bias suggested no significant difference in GDM incidence between women receiving an additional exercise intervention and routine care. Based on the limited data currently available, conclusive evidence is not available to guide practice. Larger, well-designed randomised trials, with standardised behavioural interventions are needed to assess the effects of exercise on preventing GDM and other adverse pregnancy outcomes including large-for-gestational age and perinatal mortality. Longer-term health outcomes for both women and their babies and health service costs should be included. Several such trials are in progress. We identified another seven trials which are ongoing and we will consider these for inclusion in the next update of this review. Plain language summary Exercise for pregnant women for preventing gestational diabetes mellitus Each year, a significant number of pregnant women around the world develop gestational diabetes mellitus (GDM), defined as glucose intolerance or high blood glucose concentration (hyperglycaemia) with onset or first recognition during pregnancy. During normal pregnancy, insulin becomes less effective in transferring glucose from the blood stream to the mother’s tissues to ensure
Han S, Middleton P, Shepherd E, Van Ryswyk E, Crowther CA. Different types of dietary advice for women with gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2017;2):
- Background Dietary advice is the main strategy for managing gestational diabetes mellitus (GDM). It remains unclear what type of advice is best. Objectives To assess the effects of different types of dietary advice for women with GDM for improving health outcomes for women and babies. Search methods We searched Cochrane Pregnancy and Childbirth’s Trials Register (8 March 2016), PSANZ’s Trials Registry (22 March 2016) and reference lists of retrieved studies. Selection criteria Randomised controlled trials comparing the effects of different types of dietary advice for women with GDM. Data collection and analysis Two authors independently assessed study eligibility, risk of bias, and extracted data. Evidence quality for two comparisons was assessed using GRADE, for primary outcomes for the mother: hypertensive disorders of pregnancy; caesarean section; type 2 diabetes mellitus; and child: large-for-gestational age; perinatal mortality; neonatal mortality or morbidity composite; neurosensory disability; secondary outcomes for the mother: induction of labour; perineal trauma; postnatal depression; postnatal weight retention or return to pre-pregnancy weight; and child: hypoglycaemia; childhood/adulthood adiposity; childhood/adulthood type 2 diabetes mellitus. Main results In this update, we included 19 trials randomising 1398 women with GDM, at an overall unclear to moderate risk of bias (10 comparisons). For outcomes assessed using GRADE, downgrading was based on study limitations, imprecision and inconsistency. Where no findings are reported below for primary outcomes or pre-specified GRADE outcomes, no data were provided by included trials. Primary outcomes Low-moderate glycaemic index (GI) versus moderate-high GI diet (four trials): no clear differences observed for: large-for-gestational age (risk ratio (RR) 0.71, 95% confidence interval (CI) 0.22 to 2.34; two trials, 89 infants; low-quality evidence ); severe hypertension or pre-eclampsia (RR 1.02, 95% CI 0.07 to 15.86; one trial, 95 women; very low-quality evidence ); eclampsia (RR 0.34, 95% CI 0.01 to 8.14; one trial, 83 women; very low-quality evidence ) or caesarean section (RR 0.66, 95% CI 0.29 to 1.47; one trial, 63 women; low-quality evidence ). Energy-restricted versus no energy-restricted diet (three trials): no clear differences seen for: large-for-gestational age (RR 1.17, 95% CI 0.65 to 2.12; one trial, 123 infants; low-quality evidence ); perinatal mortality (no events; two trials, 423 infants; low-quality evidence ); pre-eclampsia (RR 1.00, 95% CI 0.51 to 1.97; one trial, 117 women; low-quality evidence ); or caesarean section (RR 1.12, 95% CI 0.80 to 1.56; two trials, 420 women; low-quality evidence ). DASH (Dietary Approaches to Stop Hypertension) diet versus control diet (three trials): no clear differences observed for: pre-eclampsia (RR 1.00, 95% CI 0.31 to 3.26; three trials, 136 women); however there were fewer caesarean sections in the DASH diet group (RR 0.53, 95% CI 0.37 to 0.76; two trials, 86 women). Low-carbohydrate versus high-carbohydrate diet (two trials): no clear differences seen for: large-for-gestational age (RR 0.51, 95% CI 0.13 to 1.95; one trial, 149 infants); perinatal mortality (RR 3.00, 95% CI 0.12 to 72.49; one trial, 150 infants); maternal hypertension (RR 0.40, 95% CI 0.13 to 1.22; one trial, 150 women); or caesarean section (RR 1.29, 95% CI 0.84 to 1.99; two trials, 179 women). High unsaturated fat versus low unsaturated fat diet (two trials): no clear differences observed for: large-for-gestational age (RR 0.54, 95% CI 0.21 to 1.37; one trial, 27 infants); pre-eclampsia (no cases; one trial, 27 women); hypertensio in pregnancy (RR 0.54, 95% CI 0.06 to 5.26; one trial, 27 women); caesarean section (RR 1.08, 95% CI 0.07 to 15.50; one trial, 27 women); diabetes at one to two weeks (RR 2.00, 95% CI 0.45 to 8.94; one trial, 24 women) or four to 13 months postpartum (RR 1.00, 95% CI 0.10 to 9.61; one trial, six women). Low-GI versus high-fibre moderate-GI diet (one trial): no clear differences seen for: large-for-gestational age (RR 2.87, 95% CI 0.61 to 13.50; 92 infants); caesarean section (RR 1.91, 95% CI 0.91 to 4.03; 92 women); or type 2 diabetes at three months postpartum (RR 0.76, 95% CI 0.11 to 5.01; 58 women). Diet recommendation plus diet-related behavioural advice versus diet recommendation only (one trial): no clear differences observed for: large-for-gestational age (RR 0.73, 95%
Different types of dietary advice for women with gestational diabetes mellitus

What is the issue? Gestational diabetes mellitus (GDM) is a carbohydrate intolerance resulting in excess of sugar in the blood (hyperglycaemia) that begins or is first recognised during pregnancy. Dietary counselling or advice is the main strategy for helping women manage GDM, but it is not clear what dietary advice is best. In this review we set out to determine what dietary advice for women with GDM is best for reducing health complications for women and their babies. Why is this important? Women with GDM are at increased risk of developing high blood pressure and pre-eclampsia (high blood pressure with swelling and protein in the urine) during pregnancy. The babies can grow large for their gestational age. As a result, they may be injured at birth, or cause injury to their mothers during the birth. The babies are more likely to have their birth induced or be born by caesarean section. Both the women and their babies are at increased risk of long-term health problems including type 2 diabetes and disability. What evidence did we find? We searched the medical literature on 8 March 2016 and for this updated review we included 19 randomised controlled trials involving 1398 women with GDM and their babies. The overall risk of bias of the trials was unclear or moderate because of methodological limitations and the quality of the evidence was low or very low. The studies were generally small, few compared the same or similar interventions, and the outcomes they reported on were not comprehensive. Ten different dietary advice comparisons were included. These were: 1) a low-moderate glycaemic index (GI) diet with a moderate-high GI diet (four trials); 2) an energy-restricted diet with a diet with no energy restriction (three trials); 3) a 'Dietary Approaches to Stop Hypertension (DASH)' diet rich in fruits, vegetables, whole grains and low-fat dairy products with a control diet (three trials); 4) a low-carbohydrate diet with a high-carbohydrate diet (two trials); 5) a high unsaturated fat diet with a low unsaturated fat diet (two trials); 6) a low-GI diet with a high-fibre moderate-GI diet (one trial); 7) diet recommendations and diet-related behavioural advice with diet recommendations only (one trial); 8) a soy protein-enriched diet with a diet with no soy protein (one trial); 9) a high-fibre diet with a standard-fibre diet (one trial); and 10) an ethnic-specific diet with a standard healthy diet (one trial). The review found no clear differences between the different types of dietary advice on the number of women with high blood pressure during pregnancy including pre-eclampsia (nine trials in six different diet comparisons), large-for-gestational age babies (eight trials in seven different diet comparisons), perinatal deaths including stillbirth and death around the time of the birth (three trials in two different diet comparisons), type 2 diabetes development for the mother (two trials in two different diet comparisons), and a composite outcome of neonatal deaths or ill-health (one trial in one diet comparison). No clear difference was seen in the number of babies delivered by caesarean section (10 trials in eight different diet comparisons) except for a reduction with a DASH diet. None of the included trials reported on later disability during childhood for the babies. A range of other outcomes were looked at with no consistent differences reported between the different types of dietary advice. Outcomes related to longer-term health for women and their babies, and the use and costs of health services were largely not reported. What does this mean? Dietary advice is the main strategy for managing GDM, however it remains unclear what type of advice is best. Conclusive evidence from randomised controlled trials is not yet available to guide practice, although a wide range of dietary advice interventions have been investigated. Few trials have compared the same or similar interventions, trials have been small and have reported limited findings. Further large, well-designed, randomised controlled trials are required to assess the effects of different types of dietary advice for women with GDM for improving health outcomes for women and their babies in the short and long term.
Martis R, Brown J, Alsweiler J, Crawford TJ, Crowther CA. Different intensities of glycaemic control for women with gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2016;4:

- Background Gestational diabetes mellitus (GDM) has major short- and long-term implications for both the mother and her baby. GDM is defined as a carbohydrate intolerance resulting in hyperglycaemia or any degree of glucose intolerance with onset or first recognition during pregnancy from 24 weeks' gestation onwards and which resolves following the birth of the baby. Rates for GDM can be as high as 25% depending on the population and diagnostic criteria used and rates are increasing globally. Risk factors associated with GDM include advanced maternal age, obesity, ethnicity, family history of diabetes, and a previous history of GDM, macrosomia or unexplained stillbirth. There is wide variation internationally in glycaemic treatment target recommendations for women with GDM that are based on consensus rather than high-quality trials.

Objectives To assess the effect of different intensities of glycaemic control in pregnant women with GDM on maternal and infant health outcomes. Search methods We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 January 2016), ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) (1 February 2016) and reference lists of the retrieved studies. Selection criteria We included one randomised controlled trial. Cluster-randomised and quasi-randomised controlled trials were eligible for inclusion. Data collection and analysis We used the methods described in the Cochrane Handbook for Systematic Reviews of Interventions for carrying out data collection, assessing study quality and analysing results. Two review authors independently assessed trial eligibility for inclusion, evaluated methodological quality and extracted data for the one included study. We sought additional information from one trial author but had no response. We assessed the quality of evidence for selected outcomes using the GRADE approach. Main results We included one Canadian trial of 180 women, recruited between 20 to 32 weeks' gestation, who had been diagnosed with GDM. Data from 171 of the 180 women were published as a conference abstract and no full report has been identified. The overall risk of bias of the single included study was judged to be unclear. The included trial did not report on any of this review's primary outcomes. For the mother, these were hypertension disorders of pregnancy or subsequent development of type 2 diabetes. For the infant, our primary outcomes were (perinatal (fetal and neonatal) mortality; large-for-gestational age; composite of death or severe morbidity or later childhood neurosensory disability). The trial did report data relating to some of this review's secondary outcomes. There was no clear difference in caesarean section rates for women assigned to using strict glycaemic targets (pre-prandial 5.0 mmol/L (90 mg/dL) and at one-hour postprandial 6.7 mmol/L (120 mg/dL)) (28/85, 33%) when compared with women assigned to using liberal glycaemic targets (pre-prandial 5.8 mmol/L (103 mg/dL) and at one-hour postprandial 7.8 mmol/L (140 mg/dL)) (21/86, 24%) (risk ratio (RR) 1.35, 95% confidence interval (CI) 0.83 to 2.18, one trial, 171 women; very low quality). Using the GRADE approach, we found the quality of the evidence to be very low for caesarean section due to poor reporting of risk of bias, imprecision and publication bias. Strict glycaemic targets were associated with an increase in the use of pharmacological therapy (identified as the use of insulin in this study) (33/85; 39%) compared with liberal glycaemic targets (18/86; 21%) (RR 1.85, 95% CI 1.14 to 3.03; one trial, 171 women). CIs are wide suggesting imprecision and caution is required when interpreting the data. No other secondary maternal outcome data relevant to this review were reported. For the infant, there were no clear differences between the groups of women receiving strict and liberal glycaemic targets for macrosomia (birthweight greater than 4000 g) (RR 1.35, 95% CI 0.31 to 5.85, one trial, 17 babies); small-for-gestational age (RR 1.12, 95% CI 0.48 to 2.63, one trial, 171 babies); birthweight (mean difference (MD) -92.00 g, 95% CI -241.97 to 57.97, one trial, 171 babies) or gestational age (MD -0.30 weeks, 95% CI -0.73 to 0.13, one trial, 171 babies). Adverse effects data were not reported. No other secondary neonatal outcomes relevant to this review were reported. Authors' conclusions This review is based on a single study (involving 180 women) with an unclear risk of bias. The trial (which was only reported in a conference abstract) did not provide data for any of this review's primary outcomes but did provide data for a limited number of our secondary outcomes. There is insufficient evidence to guide clinical practice for targets for glycaemic control for women with GDM to minimise adverse effects on maternal and fetal health. Glycaemic target recommendations from international professional organisations for maternal glycaemic control vary widely and are reliant on consensus given the lack of high-quality evidence. Further high-quality trials are needed, and these should compare different glycaemic targets for guiding treatment of women with GDM, assess both short-term and long-term health outcomes for women and their babies, include women's experiences and assess health services costs. Four studies are ongoing. Plain language summary What is the most effective blood sugar range to guide treatment for women who develop gestational diabetes mellitus (GDM) in their pregnancy? What is the issue? Up to a quarter of pregnant women develop gestational diabetes mellitus (GDM) depending on their ethnicity and the diagnostic criteria used. GDM is evident as high blood sugar levels (hyperglycaemia) during pregnancy and is associated with an increased risk of developing high blood pressure (hypertension) and protein in the urine during pregnancy (pre-eclampsia). These women are more likely to have a caesarean birth, develop type 2 diabetes, postnatal depression, and cardiovascular
disease later on in life. The high blood sugar levels that are associated with GDM often return to normal as soon as the baby is born, but women with GDM are at risk of again developing GDM in future pregnancies. Babies whose mothers have been diagnosed with GDM are at an increased risk of having a birthweight greater than 4000 g, increased risk of birth trauma because of their size and developing breathing difficulties after birth. The babies are also at risk of future obesity and type 2 diabetes. Why is this important? Women with GDM are treated with the aims of controlling high maternal blood sugar levels and reducing the risks of GDM for the mother and the baby. Blood sugar control is monitored by measuring blood sugar concentrations to ensure they are maintained within a pre-defined level or range. The blood sugar results are usually obtained by the mother using a finger prick to collect a drop of her blood on a test strip, which is inserted into a small machine (a glucometer) that reads the sugar level of the blood on the test strip. The glucometer reading alerts the pregnant woman to her current blood sugar level and is used to guide her treatment. For example, how many units of insulin she requires before eating. However, it is currently unclear how to advise pregnant women with newly diagnosed GDM what is the most effective blood sugar range to aim for and guide treatment. What evidence did we find? We searched for evidence on 31 January 2016 and found one small randomised controlled trial (abstract only) that was of poor quality and involved 180 women from Canada. The trial compared two blood sugar ranges, one strict the other more liberal, and reported a very few health outcomes for the pregnant woman and her baby. The trial did not provide any data for this review’s main outcomes. For the woman, these related to the development of high blood pressure and protein in the urine during pregnancy, developing type 2 diabetes. For the baby, these outcomes related to death of the baby, increased birthweight, increased risk of birth trauma because of their size, and disability. More women were on insulin in the strictly controlled group (but this result is based on very low quality evidence). No clear differences were reported for caesarian section rates. No other secondary outcome data for women with GDM relevant to this review were reported. No differences were reported for the number of babies that had a birthweight greater than 4000 g or were small-for-gestational age. No other secondary outcomes for the babies relevant to this review were reported. The study did not report on adverse events. What does this mean? This review found that there is not yet enough evidence from randomised controlled trials to determine the best blood sugar range for improving health for pregnant women with GDM and their babies. Four studies are ongoing but not yet complete. More high-quality studies are needed that compare different targets for blood sugar levels and assess both short-term and long-term health outcomes for women and their babies to guide treatment. Studies should include women’s experiences and assess health services costs.

Martis R, Crowther CA, Shepherd E, Alsweiler J, Downie MR, Brown J. Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews. Cochrane Database of Systematic Reviews 2018;8):

- Background Successful treatments for gestational diabetes mellitus (GDM) have the potential to improve health outcomes for women with GDM and their babies. Objectives To provide a comprehensive synthesis of evidence from Cochrane systematic reviews of the benefits and harms associated with interventions for treating GDM on women and their babies. Methods We searched the Cochrane Database of Systematic Reviews (5 January 2018) for reviews of treatment/management for women with GDM. Reviews of pregnant women with pre-existing diabetes were excluded. Two overview authors independently assessed reviews for inclusion, quality (AMSTAR; ROBIS), quality of evidence (GRADE), and extracted data. Main results We included 14 reviews. Of these, 10 provided relevant high-quality and low-risk of bias data (AMSTAR and ROBIS) from 128 randomised controlled trials (RCTs), 27 comparisons, 17,984 women, 16,305 babies, and 1441 children. Evidence ranged from high- to very low-quality (GRADE). Only one effective intervention was found for treating women with GDM. Effective Lifestyle versus usual care Lifestyle intervention versus usual care probably reduces large-for-gestational age (risk ratio (RR) 0.60, 95% confidence interval (CI) 0.50 to 0.71; 6 RCTs, N = 2994; GRADE moderate-quality). Promising No evidence for any outcome for any comparison could be classified to this category. Ineffective or possibly harmful Lifestyle intervention versus usual care Lifestyle intervention versus usual care probably increases the risk of induction of labour (IOL) suggesting possible harm (average RR 1.20, 95% CI 0.99 to 1.46; 4 RCTs, N = 2699; GRADE moderate-quality). Exercise versus control Exercise intervention versus control for return to pre-pregnancy weight suggested ineffectiveness (body mass index, BMI) MD 0.11 kg/m², 95% CI -1.04 to 1.26; 3 RCTs, N = 254; GRADE moderate-quality). Insulin versus oral therapy Insulin intervention versus oral therapy probably increases the risk of IOL suggesting possible harm (RR 1.3, 95% CI 0.96 to 1.75; 3 RCTs, N = 348; GRADE moderate-quality). Probably ineffective or harmful interventions Insulin versus oral therapy probably increases the risk of IOL suggesting possible harm (RR 1.3, 95% CI 0.96 to 1.75; 3 RCTs, N = 348; GRADE moderate-quality). Inconclusive Lifestyle versus usual care The evidence for childhood adiposity kg/m² (RR 0.91, 95% CI 0.75 to 1.11; 3 RCTs, N = 767; GRADE moderate-quality) and hypoglycaemia was inconclusive (average RR 0.99, 95% CI 0.65 to 1.52; 6 RCTs, N = 3000; GRADE moderate-quality). Exercise versus control The evidence for caesarean section (RR 0.86, 95% CI 0.63 to
1.16; 5 RCTs, N = 316; GRADE moderate quality) and perinatal death or serious morbidity composite was inconclusive (RR 0.56, 95% CI 0.12 to 2.61; 2 RCTs, N = 169; GRADE moderate-quality). Insulin versus oral therapy. The evidence for the following outcomes was inconclusive: pre-eclampsia (RR 1.14, 95% CI 0.86 to 1.52; 10 RCTs, N = 2060), caesarean section (RR 1.03, 95% CI 0.93 to 1.14; 17 RCTs, N = 1988), large-for-gestational age (average RR 1.01, 95% CI 0.76 to 1.35; 13 RCTs, N = 2352), and perinatal death or serious morbidity composite (RR 1.03; 95% CI 0.84 to 1.26; 2 RCTs, N = 760). GRADE assessment was moderate-quality for these outcomes. Insulin versus diet. The evidence for perinatal mortality was inconclusive (RR 0.74, 95% CI 0.41 to 1.33; 4 RCTs, N = 1137; GRADE moderate-quality). Insulin versus insulin. The evidence for insulin aspart versus lispro for risk of caesarean section was inconclusive (RR 1.00, 95% CI 0.91 to 1.09; 3 RCTs, N = 410; GRADE moderate quality). No conclusions possible. No conclusions were possible for: lifestyle versus usual care (perineal trauma, postnatal depression, neonatal adiposity, number of antenatal visits/admissions); diet versus control (pre-eclampsia, caesarean section); myo-inositol versus placebo (hypoglycaemia); metformin versus glibenclamide (hypertensive disorders of pregnancy, pregnancy-induced hypertension, death or serious morbidity composite, insulin versus oral therapy (development of type 2 diabetes); intensive management versus routine care (IOL, large-for-gestational age); post- versus pre-prandial glucose monitoring (large-for-gestational age). The evidence ranged from moderate-, low- and very low-quality. Authors' conclusions. Currently there is insufficient high-quality evidence about the effects on health outcomes of relevance for women with GDM and their babies for many of the comparisons in this overview comparing treatment interventions for women with GDM. Lifestyle changes (including as a minimum healthy eating, physical activity and self-monitoring of blood sugar levels) was the only intervention that showed possible health improvements for women and their babies. Lifestyle interventions may result in fewer babies being large. Conversely, in terms of harms, lifestyle interventions may also increase the number of inductions. Taking insulin was also associated with an increase in hypertensive disorders, when compared to oral therapy. There was very limited information on long-term health and health services costs. Further high-quality research is needed. Plain language summary. Treatments to improve pregnancy outcomes for women who develop diabetes during pregnancy: an overview of Cochrane systematic reviews. What is the issue? The aim of this Cochrane overview was to provide a summary of the effects of interventions for women who develop diabetes during pregnancy (gestational diabetes mellitus, GDM) and the effects on women's health and the health of their babies. We assessed all relevant Cochrane Reviews (date of last search: January 2018). Why is this important? GDM can occur in mid-to-late pregnancy. High blood glucose levels (hyperglycaemia) possibly have negative effects on both the woman and her baby's health in the short- and long-term. For women, GDM can mean an increased risk of developing high blood pressure and protein in the urine (pre-eclampsia). Women with GDM also have a higher chance of developing type 2 diabetes, heart disease, and stroke later in life. Babies born to mothers with GDM are at increased risk of being large, having low blood glucose (hypoglycaemia) after birth, and yellowing of the skin and eyes (jaundice). As these babies become children, they are at higher risk of being overweight and developing type 2 diabetes. Several Cochrane Reviews have assessed different interventions for women with GDM. This overview brings these reviews together. We looked at diet, exercise, drugs, supplements, lifestyle changes, and ways GDM is managed or responded to by the healthcare team. What evidence did we find? We found 14 Cochrane systematic reviews and included 10 reviews covering 128 studies in our analysis, which included a total of 17,984 women, and their babies. The quality of the evidence ranged from very low to high. We looked at: • Dietary interventions (including change to low or moderate glycaemic index (GI) diet, calorie restrictions, low carbohydrate diet, high complex carbohydrate diet, high saturated fat diet, high fibre diet, soy-protein enriched diet, etc.) We found there were not enough data on any one dietary intervention to be able to say whether it helped or not. • Exercise programmes (including brisk walking, cycling, resistance circuit-type training, instruction on active lifestyle, home-based exercise programme, 6-week or 10-week exercise programme, yoga, etc.) Similarly, there were not enough data on any specific exercise regimen to say if it helped or not. • Taking insulin or other drugs to control diabetes (including insulin and oral glucose lowering drugs). Insulin probably increases the risk of high blood pressure and its problems in pregnancy (hypertensive disorders of pregnancy) when compared to oral therapy (moderate-quality evidence). • Supplements (myo-inositol given as a water-soluble powder or capsule). We found there was not enough data to be able to say if myo-inositol was helpful or not. • Lifestyle changes which combine two or more interventions such as: healthy eating, exercise, education, mindfulness eating (focusing the mind on eating), yoga, relaxation, etc. Lifestyle interventions may be associated with fewer babies being born large (moderate-quality evidence) but may result in an increase in inductions of labour (moderate-quality evidence). • Management strategies (including early birth, methods of blood glucose monitoring). We found little data for strategies which included planned induction of labour or planned birth by caesarean section, and there was no clear difference in outcomes among these care plans. Similarly, we found no clear difference among outcomes for different methods of blood glucose monitoring. What does this mean? There are limited data on the various interventions. Lifestyle changes (including as a minimum healthy eating, physical activity, and self-monitoring of blood sugar levels)
Reminder systems for women with previous gestational diabetes mellitus to increase uptake of testing for type 2 diabetes or impaired glucose tolerance. Cochrane Database of Systematic Reviews 2014;3:

Background The early postpartum period is an important time in which to identify the risk of diabetes in women with a history of gestational diabetes mellitus (GDM). Oral glucose tolerance and other tests can help guide lifestyle management and monitoring to reduce the future risk of type 2 diabetes mellitus. Objectives To assess whether reminder systems increase the uptake of testing for type 2 diabetes or impaired glucose tolerance in women with a history of GDM. Search methods We searched MEDLINE and EMBASE (last searched 1 June 2013) and The Cochrane Library (last searched April 2013). Selection criteria We included randomised trials of women who had experienced GDM in the index pregnancy and who were then sent any modality of reminder (or control) to complete a test for type 2 diabetes after giving birth. Data collection and analysis Two authors independently screened titles and abstracts for relevance. One author extracted the data, carried out 'Risk of bias' assessments and evaluated the overall study quality according to GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria; the other author double-checked these procedures. Meta-analysis was not possible as only one study was eligible for inclusion. Main results Only one trial with an unclear risk of bias in the majority of domains was included in the study; the overall study quality was judged to be low. This factorial trial of 256 women compared three types of postal reminder strategies (in a total of 213 women) with usual care (no postal reminder, 43 women) and reported on the uptake of four possible types of glucose tests. The three strategies investigated were: reminders sent to both the woman and the physician; reminder sent to the woman only; and reminder sent to the physician only, all issued approximately three months after the woman had given birth. There was low-quality evidence that all three reminder interventions increased uptake of oral glucose tolerance tests compared with usual care (no reminder system): reminders to the woman and the physician (uptake 60% versus 14%): risk ratio 4.23 (95% confidence interval (CI) 1.85 to 9.71); 116 participants); reminder to the woman only (uptake 55% versus 14%): RR 3.87 (95% CI 1.68 to 8.93); 111 participants); reminder to the physician only (uptake 52% versus 14%): RR 3.61 (95% CI 1.50 to 8.71); 66 participants). This represented an increase in uptake from 14% in the no reminder group to 57% across the three reminder groups. There was also an increase in uptake of fasting glucose tests in the reminder group compared with the usual care group: reminders to the woman and the physician versus no reminder (uptake 63% versus 40%): RR 1.57 (95% CI 1.01 to 2.44); reminder to the woman only (uptake 71% versus 40%): RR 1.78 (95% CI 1.16 to 2.73); reminder to the physician only (uptake 68% versus 40%): RR 1.69 (95% CI 1.06 to 2.72). Uptake of random glucose and glycated haemoglobin A1c tests was low, and no statistically significant differences were seen between the reminder and no reminder groups for these tests. Uptake of any test was higher in each of the reminder groups compared with the no reminder group (RR 1.65 (95% CI 1.12 to 2.41); 1.73 (95% CI 1.18 to 2.52); and 1.55 (95% CI 1.01 to 2.38) in the respective reminder groups. The trial did not report this review’s other primary outcomes (proportion of women diagnosed with type 2 diabetes or showing impaired glucose tolerance or impaired fasting glucose after giving birth; or health-related quality of life). Nor did it report any secondary review outcomes such as diabetes-associated morbidity, lifestyle changes, need for insulin, recurrence of GDM or women's and/or health professionals’ views of the intervention. No adverse events of the intervention were reported. Subgroup interaction tests gave no indication that dual reminders (to both women and physicians) were more successful than single reminders to either women or physicians alone. It was also not clear if test uptakes between women in the reminder and no reminder groups differed by type of glucose test undertaken. Authors’ conclusions Results from the only trial that fulfilled our inclusion criteria showed low-quality evidence for a marked increase in the uptake of testing for type 2 diabetes in women with previous GDM following the issue of postal reminders. The effects of other forms of reminder systems need to be assessed to see whether test uptake also increases when email and telephone reminders are deployed. We also need a better understanding of why some women fail to take opportunities to be screened postpartum. As the ultimate aim of increasing postpartum testing is to prevent the subsequent development of type 2 diabetes, it is important to determine whether increased test uptake rates also increase women's use of preventive strategies such as lifestyle modifications. Plain language summary Reminder systems for women with previous gestational diabetes mellitus to increase uptake of testing for type 2 diabetes or impaired glucose tolerance Review question To assess the effects of reminder systems to increase uptake of testing for type 2 diabetes or impaired glucose tolerance in women with a history of gestational diabetes mellitus (GDM). Background Some
women experience high blood glucose concentrations during pregnancy (termed GDM). Although these high blood glucose concentrations usually normalise immediately after birth, women who have experienced GDM are at an increased risk of developing type 2 diabetes in the future. It is therefore important that they are regularly tested for higher than normal blood glucose levels (to detect type 2 diabetes or 'impaired glucose tolerance' which is a prediabetic state sometimes preceding type 2 diabetes), starting in the months after they have given birth. However, for a variety of reasons, many women do not get their blood glucose tested after experiencing GDM. Study characteristics A single study of 256 women who had experienced GDM whether posting reminder letters to 213 women or their doctors, three months after the birth of a baby, would help to increase the number of women taking a blood glucose test compared with 43 women sent no reminder. Key results This study showed that, compared with no reminder, a postal reminder was around two to four times (depending on the blood glucose test concerned) more likely to encourage women who had experienced GDM to take a blood glucose test three months after having their baby. It did not seem to make a difference if the reminder was sent to the woman only, the physician only or to both the woman and the physician. The trial did not assess women's quality of life, or how many women were subsequently diagnosed with type 2 diabetes or impaired glucose results after giving birth. Other kinds of reminders such as email and telephone need to be assessed in studies as they might be easier and more convenient for women than posted reminders. We need to know more about women's preferences and attitudes, and also to find out whether increasing the chances of a woman being tested helps to reduce her risk of developing type 2 diabetes in the future, for example by encouraging a healthier diet and more exercise. Quality of the evidence The overall quality of evidence was considered low as the only included study involved few numbers of participants and provided imprecise results. Currentness of data This evidence is up to date as of June 2013.

Middleton P, Crowther CA, Simmonds L. Different intensities of glycaemic control for pregnant women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2016;5;
- Background The optimal glycaemic control target in pregnant women with pre-existing diabetes is unclear, although there is a clear link between high glucose concentrations and adverse birth outcomes. Objectives To assess the effects of different intensities of glycaemic control in pregnant women with pre-existing type 1 or type 2 diabetes. Search methods We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 January 2016) and planned to search reference lists of retrieved studies. Selection criteria We included randomised controlled trials comparing different glycaemic control targets in pregnant women with pre-existing diabetes. Data collection and analysis Two review authors independently assessed trials for inclusion, conducted data extraction, assessed risk of bias and checked for accuracy. We assessed the quality of the evidence using the GRADE approach. Main results We included three trials, all in women with type 1 diabetes (223 women and babies). All three trials were at high risk of bias due to lack of blinding, unclear methods of randomisation and selective reporting of outcomes. Two trials compared very tight (3.33 to 5.0 mmol/L fasting blood glucose (FBG)) with tight-moderate (4.45 to 6.38 mmol/L) glycaemic control targets, with one trial of 22 babies reporting no perinatal deaths or serious perinatal morbidity ( evidence graded low for both outcomes ) . In the same trial, there were two congenital anomalies in the very tight, and none in the tight-moderate group, with no significant differences in caesarean section between groups (risk ratio (RR) 0.92, 95% confidence interval (CI) 0.49 to 1.73; evidence graded very low ). In these two trials, glycaemic control was not significantly different between the very tight and tight-moderate groups by the third trimester, although one trial of 22 women found significantly less maternal hypoglycaemia in the tight-moderate group. In a trial of 60 women and babies comparing tight (≤ 5.6 mmol/L FBG); moderate (5.6 to 6.7 mmol/L); and loose (6.7 to 8.9 mmol/L) glycaemic control targets, there were two neonatal deaths in the loose and none in the tight or moderate groups ( evidence graded very low ) . There were significantly fewer women with pre-eclampsia ( evidence graded low ) , fewer caesarean sections ( evidence graded low ) and fewer babies with birthweights greater than 90th centile ( evidence graded low ) in the combined tight-moderate compared with the loose group. The quality of the evidence was graded low or very low for important outcomes, because of design limitations to the studies, the small numbers of women included, and wide confidence intervals crossing the line of no effect. Many of the important outcomes were not reported in these studies. Authors' conclusions In a very limited body of evidence, few differences in outcomes were seen between very tight and tight-moderate glycaemic control targets in pregnant women with pre-existing type 1 diabetes, including actual glycaemic control achieved. There is evidence of harm (increased pre-eclampsia, caesareans and birthweights greater than 90th centile) for 'loose' control (FBG above 7 mmol/L). Future trials comparing interventions, rather than glycaemic control targets, may be more feasible. Trials in pregnant women with pre-existing type 2 diabetes are required. Plain language summary What is the best blood glucose target for pregnant women who have type 1 or type 2 diabetes before becoming pregnant? What is the issue? Pregnant women with diabetes need to keep their blood glucose levels stable, using diet, exercise, insulin or other drugs, clinic visits and monitoring. This review looked at the best blood glucose target for pregnant women with diabetes. Why is this important? Women who have either type 1 or type 2 diabetes
Moy FM, Ray A, Buckley BS, West HM. Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2017(6):

- Background Self-monitoring of blood glucose (SMBG) is recommended as a key component of the management plan for diabetes therapy during pregnancy. No existing systematic reviews consider the benefits/effectiveness of various techniques of blood glucose monitoring on maternal and infant outcomes among pregnant women with pre-existing diabetes. The effectiveness of the various monitoring techniques is unclear. Objectives To compare techniques of blood glucose monitoring and their impact on maternal and infant outcomes among pregnant women with pre-existing diabetes. Search methods We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 November 2016), searched reference lists of retrieved studies and contacted trial authors. Selection criteria Randomised controlled trials (RCTs) and quasi-RCTs comparing techniques of blood glucose monitoring including SMBG, continuous glucose monitoring (CGM) or clinic monitoring among pregnant women with pre-existing diabetes mellitus (type 1 or type 2). Trials investigating timing and frequency of monitoring were also included. RCTs using a cluster-randomised design were eligible for inclusion but none were identified. Data collection and analysis Two review authors independently assessed study eligibility, extracted data and assessed the risk of bias of included studies. Data were checked for accuracy. The quality of the evidence was assessed using the GRADE approach. Main results This review update includes at total of 10 trials (538 women (468 women with type 1 diabetes and 70 women with type 2 diabetes). The trials took place in Europe and the USA. Five of the 10 included studies were at moderate risk of bias, four studies were at low to moderate risk of bias, and one study was at high risk of bias. The trials are too small to show differences in important outcomes such as macrosomia, preterm birth, miscarriage or death of baby. Almost all the reported GRADE outcomes were assessed as being very low-quality evidence. This was due to design limitations in the studies, wide confidence intervals, small sample sizes, and few events. In addition, there was high heterogeneity for some outcomes. Various methods of glucose monitoring were compared in the trials. Neither pooled analyses nor individual trial analyses showed any clear advantages of one monitoring technique over another for primary and secondary outcomes. Many important outcomes were not reported. 1. Self-monitoring versus standard care (two studies, 43 women): there was no clear difference for caesarean section (risk ratio (RR) 0.78, 95% confidence interval (CI) 0.40 to 1.49; one study, 28 women) or glycaemic control (both very low-quality), and not enough evidence to assess perinatal mortality and neonatal mortality and morbidity composite.

Hypertensive disorders of pregnancy, large-for-gestational age, neurosensory disability, and preterm birth were not reported in either study. 2. Self-monitoring versus hospitalisation (one study, 100 women): there was no clear difference for hypertensive disorders of pregnancy (pre-eclampsia and hypertension) (RR 4.26, 95% CI 0.52 to 35.16; very low-quality: RR 0.43, 95% CI 0.08 to 2.22; very low-quality). There was no clear difference in caesarean section or preterm birth less than 37 weeks' gestation (both very low quality), and the sample size was too small to assess perinatal mortality (very low-quality). Large-for-gestational age, mortality or morbidity composite, neurosensory disability and preterm birth less than 34 weeks were not reported. 3. Pre-prandial versus post-prandial glucose monitoring (one study, 61 women): there was no clear difference between groups for caesarean section (RR 1.45, 95% CI 0.92 to 2.28; very low-quality), large-for-gestational age (RR 1.16, 95% CI 0.73 to 1.85; very low-quality) or glycaemic control (very low-quality). The results for hypertensive disorders of pregnancy: pre-eclampsia and perinatal mortality are not meaningful because these outcomes were too rare to show differences in a small sample (very low-quality). The study
did not report the outcomes mortality or morbidity composite, neurosensory disability or preterm birth. 4.
Automated telemedicine monitoring versus conventional system (three studies, 84 women); there was no clear
difference for caesarean section (RR 0.96, 95% CI 0.62 to 1.48; one study, 32 women; very low-quality).
Automated telemedicine monitoring versus conventional system, continuous monitoring versus standard
monitoring versus standard care, self-monitoring or the use of special equipment that can continuously
monitor blood glucose during pregnancy in order to control blood glucose levels and so reduce problems
for babies and mothers. We collected and analysed all relevant studies to answer this question (search date:
November 2016). Why is this important? Diabetes can cause problems for pregnant women and their babies,
including early births, large babies, difficult births and the need for caesarean section. The problems also
include a risk to the baby of bleeding in the brain (intracranial haemorrhage), and during labour, there is an
increased risk of the baby’s shoulder becoming stuck (shoulder dystocia). After the birth, there is an increased
risk of low blood sugar (hypoglycaemia), jaundice and breathing problems. The babies are more likely to be
admitted to an intensive care unit. Late, there is an increased risk of the baby developing diabetes as a child.
Women with existing diabetes that is not well-controlled at the time of conception and in the first three months
of pregnancy are at increased risk of miscarriage, of having a baby with developmental problems or stillbirth.
Several methods for monitoring blood glucose levels are used including regular testing at antenatal clinics,
self-monitoring, or the use of special equipment that can continuously monitor glucose levels during
pregnancy. A more accurate measure of blood sugar may lead to more effective control of blood glucose and
a reduction in the potential problems for babies and mothers. What evidence did we find? We found 10 trials
involving 538 women and babies. We found studies that compared various methods of glucose monitoring:
self-monitoring versus standard care, self-monitoring versus hospitalisation, monitoring before meals versus
monitoring after meals, glucose monitoring, automated monitoring versus conventional system, continuous
glucose monitoring (CGM) versus intermittent monitoring and constant CGM versus intermittent CGM. The
trials were from European countries and the USA. They looked at different techniques of monitoring and
reported on different outcomes. The number of women in each study was generally small. The evidence was
mostly of very low-quality, so we cannot be certain of the results. The results did not show that any one
monitoring technique was better than others. There was no clear difference between the monitoring
techniques when mothers’ control of blood glucose or high blood pressure disorders were looked at. Similarly,
we found no difference in rates of caesarean section, the number of large babies, the number of babies who
died or had serious health problems, or the number of babies being born too early (preterm). We do not know
if this is because there is no difference between the techniques, or if there is a difference that these studies
did not manage to show. What does this mean? The review showed that there is not enough evidence to say
with any certainty which monitoring method for blood glucose is best. More research is needed to find out
which monitoring method, if any, is best at reducing the risk of complications.
Muktabhant B, Lawrie TA, Lumbiganon P, Laopaiboon M. Diet or exercise, or both, for preventing excessive weight gain in pregnancy. Cochrane Database of Systematic Reviews 2015;6:CD007145

BACKGROUND: This is an update of a Cochrane review first published in 2012, Issue 4. Excessive weight gain during pregnancy is associated with poor maternal and neonatal outcomes including gestational diabetes, hypertension, caesarean section, macrosomia, and stillbirth. Diet or exercise interventions, or both, may reduce excessive gestational weight gain (GWG) and associated poor outcomes; however, evidence from the original review was inconclusive.

OBJECTIVES: To evaluate the effectiveness of diet or exercise, or both, interventions for preventing excessive weight gain during pregnancy and associated pregnancy complications.

SEARCH METHODS: We searched the Cochrane Pregnancy and Childbirth Group’s Trials Register (5 November 2014), contacted investigators of the previously identified ongoing studies and scanned reference lists of retrieved studies.

SELECTION CRITERIA: Randomised controlled trials (RCTs) of diet or exercise, or both, interventions for preventing excessive weight gain in pregnancy.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. We organised RCTs according to the type of interventions and pooled data using the random-effects model in the Review Manager software. We also performed subgroup analyses according to the initial risk of adverse effects related to poor weight control. We performed sensitivity analysis to assess the robustness of the findings.

MAIN RESULTS: We included 65 RCTs, out of which 49 RCTs involving 11,444 women contributed data to quantitative meta-analysis. Twenty studies were at moderate-to-high risk of bias. Study interventions involved mainly diet only, exercise only, and combined diet and exercise interventions, usually compared with standard care. Study methods varied widely; therefore, we estimated the average effect across studies and performed sensitivity analysis, where appropriate, by excluding outliers and studies at high risk of bias. Diet or exercise, or both, interventions reduced the risk of excessive GWG on average by 20% overall (average risk ratio (RR) 0.80, 95% confidence interval (CI) 0.73 to 0.87; participants = 7096; studies = 24; I² = 52%). This estimate was robust to sensitivity analysis, which reduced heterogeneity, therefore we graded this evidence as high-quality. Interventions involving low glycaemic load diets, supervised or unsupervised exercise only, or diet and exercise combined all led to similar reductions in the number of women gaining excessive weight in pregnancy. Women receiving diet or exercise, or both interventions were more likely to experience low GWG than those in control groups (average RR 1.14, 95% CI 1.02 to 1.27; participants = 4422; studies = 11; I² = 3%; moderate-quality evidence). We found no difference between intervention and control groups with regard to pre-eclampsia (RR 0.95, 95% CI 0.77 to 1.16; participants = 5330; studies = 15; I² = 0%; high-quality evidence); however, maternal hypertension (not a pre-specified outcome) was reduced in the intervention group compared with the control group overall (average RR 0.70, 95% CI 0.51 to 0.96; participants = 5162; studies = 11; I² = 43%; low-quality evidence). There was no clear difference between groups with regard to caesarean delivery overall (RR 0.95, 95% CI 0.88 to 1.03; participants = 7534; studies = 28; I² = 9%; high-quality evidence); although the effect estimate suggested a small difference (5%) in favour of the interventions. In addition, for combined diet and exercise counselling interventions there was a 13% (-1% to 25%) reduction in this outcome (borderline statistical significance). We found no difference between groups with regard to preterm birth overall (average RR 0.91, 95% CI 0.68 to 1.22; participants = 5923; studies = 16; I² = 16%; moderate-quality evidence); however limited evidence suggested that these effect estimates may differ according to the types of interventions, with a trend towards an increased risk for exercise-only interventions. We found no clear difference between intervention and control groups with regard to infant macrosomia (average RR 0.93, 95% CI 0.86 to 1.02; participants = 8598; studies = 27; I² = 0%; high-quality evidence), although the effect estimate suggested a small difference (7% reduction) in favour of the intervention group. The largest effect size occurred in the supervised exercise-only intervention group (RR 0.81, 95% CI 0.64 to 1.02; participants = 2445; studies = 7; I² = 0%), which approached statistical significance (P = 0.07). Furthermore, in subgroup analysis by risk, high-risk women (overweight or obese women, or women with or at risk of gestational diabetes) receiving combined diet and exercise counselling interventions experienced a 15% reduced risk of infant macrosomia (average RR 0.85, 95% CI 0.73 to 1.00; participants = 3252; studies = nine; I² = 0; P = 0.05; moderate-quality evidence). There were no differences in the risk of poor neonatal outcomes including shoulder dystocia, neonatal hypoglycaemia, hyperbilirubinaemia, or birth trauma (all moderate-quality evidence) between intervention and control groups; however, infants of high-risk women had a reduced risk of respiratory distress syndrome if their mothers were in the intervention group (RR 0.47, 95% CI 0.26 to 0.85; participants = 2256; studies = two; I² = 0%; moderate-quality evidence).

AUTHORS’ CONCLUSIONS: High-quality evidence indicates that diet or exercise, or both, during pregnancy can reduce the risk of excessive GWG. Other benefits may include a lower risk of caesarean delivery, macrosomia, and neonatal respiratory morbidity, particularly for high-risk women receiving combined diet and exercise interventions. Maternal hypertension may also be reduced. Exercise appears to be an important part of the interventions. We performed sensitivity analysis to assess the robustness of the findings.
of controlling weight gain in pregnancy and more research is needed to establish safe guidelines. Most included studies were carried out in developed countries and it is not clear whether these results are widely applicable to lower income settings.

O'Neill SM, Kenny LC, Khashan AS, West HM, Smyth RMD, Kearney PM. Different insulin types and regimens for pregnant women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2017;2):

- Background Insulin requirements may change during pregnancy, and the optimal treatment for pre-existing diabetes is unclear. There are several insulin regimens (e.g. via syringe, pen) and types of insulin (e.g. fast-acting insulin, human insulin). Objectives To assess the effects of different insulin types and different insulin regimens in pregnant women with pre-existing type 1 or type 2 diabetes. Search methods We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 October 2016), ClinicalTrials.gov (17 October 2016), the WHO International Clinical Trials Registry Platform (ICTRP; 17 October 2016), and the reference lists of retrieved studies. Selection criteria We included randomised controlled trials (RCTs) that compared different insulin types and regimens in pregnant women with pre-existing diabetes. We had planned to include cluster-RCTs, but none were identified. We excluded quasi-randomised controlled trials and cross-over trials. We included studies published in abstract form and contacted the authors for further details when applicable. Conference abstracts were superseded by full publications. Data collection and analysis Two review authors independently assessed trials for inclusion, conducted data extraction, assessed risk of bias, and checked for accuracy. We assessed the quality of the evidence using the GRADE approach. Main results The findings in this review were based on very low-quality evidence, from single, small sample sized trial estimates, with wide confidence intervals (CI), some of which crossed the line of no effect; many of the prespecified outcomes were not reported. Therefore, they should be interpreted with caution. We included five trials that included 554 women and babies (four open-label, multi-centre, two-arm trials; one single centre, four-arm RCT). All five trials were at a high or unclear risk of bias due to lack of blinding, unclear methods of randomisation, and selective reporting of outcomes. Pooling of data from the trials was not possible, as each trial looked at a different comparison. 1. One trial (N = 33 women) compared Lispro insulin with regular insulin and provided very low-quality evidence for the outcomes. There were seven episodes of pre-eclampsia in the Lispro group and nine in the regular insulin group, with no clear difference between the two groups (risk ratio (RR) 0.68, 95% CI 0.35 to 1.30). There were five caesarean sections in the Lispro group and nine in the regular insulin group, with no clear difference between the two groups (RR 0.59, 95% CI 0.25 to 1.39). There were no cases of fetal anomaly in the Lispro group and one in the regular insulin group, with no clear difference between the groups (RR 0.35, 95% CI 0.02 to 8.08). Macrosomia, perinatal deaths, episodes of birth trauma including shoulder dystocia, nerve palsy, and fracture, and the composite outcome measure of neonatal morbidity were not reported. 2. One trial (N = 42 women) compared human insulin to animal insulin, and provided very low-quality evidence for the outcomes. There were no cases of macrosomia in the human insulin group and two in the animal insulin group, with no clear difference between the groups (RR 0.22, 95% CI 0.01 to 4.30). Perinatal death, pre-eclampsia, caesarean section, fetal anomaly, birth trauma including shoulder dystocia, nerve palsy and fracture and the composite outcome measure of neonatal morbidity were not reported. 3. One trial (N = 93 women) compared pre-mixed insulin (70 NPH/30 REG) to self-mixed, split-dose insulin and provided very low-quality evidence to support the outcomes. Two cases of macrosomia were reported in the pre-mixed insulin group and four in the self-mixed insulin group, with no clear difference between the two groups (RR 0.49, 95% CI 0.09 to 2.54). There were seven cases of caesarean section (for cephalo-pelvic disproportion) in the pre-mixed insulin group and 12 in the self-mixed insulin group, with no clear difference between groups (RR 0.57, 95% CI 0.25 to 1.32). Perinatal death, pre-eclampsia, fetal anomaly, birth trauma including shoulder dystocia, nerve palsy, or fracture and the composite outcome measure of neonatal morbidity were not reported. 4. In the same trial (N = 93 women), insulin injected with a Novolin pen was compared to insulin injected with a conventional needle (syringe), which provided very low-quality evidence to support the outcomes. There was one case of macrosomia in the pen group and five in the needle group, with no clear difference between the different insulin regimens (RR 0.21, 95% CI 0.03 to 1.76). There were five deliveries by caesarean section in the pen group compared with 14 in the needle group; women were less likely to deliver via caesarean section when insulin was injected with a pen compared to a conventional needle (RR 0.38, 95% CI 0.15 to 0.97). Perinatal death, pre-eclampsia, fetal anomaly, birth trauma including shoulder dystocia, nerve palsy, or fracture, and the composite outcome measure of neonatal morbidity were not reported. 5. One trial (N = 223 women) comparing insulin Aspart with human insulin reported none of the review's primary outcomes: macrosomia, perinatal death, pre-eclampsia, caesarean section, fetal anomaly, birth trauma including shoulder dystocia, nerve palsy, or fracture, or the composite outcome measure of neonatal morbidity. 6. One trial (N = 162 women) compared insulin Detemir with NPH insulin, and supported the outcomes with very low-quality evidence. There were three cases of major fetal anomalies in the insulin
Incorporating adequate lin eot measure view's main outcomes. All five others and babies We searched the Cochrane Pregnancy and Childbirth Group Trials Register (30 September 2016) and review is to compare the effects of different methods and settings for glucose monitoring for women with GDM which can be car recommended by healthcare professionals. There are several different methods for monitoring blood glucose regimen was best for pregnant women with pre-existing diabetes? What is the issue? The insulin needs of pregnant women with type 1 or 2 diabetes change during pregnancy. Insulin is available in many forms, which affect how often and when the insulin is given. These forms vary in the time needed before the insulin has its effect, how long the effect may last, and whether it is made from animals or humans, which may be important personally or culturally. This review looked at the safest and most effective types and ways of giving insulin during pregnancy. Why is this important? Women with type 1 or 2 diabetes are at increased risk of complications during pregnancy and birth. They are more likely to experience pregnancy loss (stillbirth, miscarriage), high blood pressure and pre-eclampsia (high blood pressure associated with swelling and protein in the urine), and have large babies (called macrosomia, when the baby is 4 kg or more at birth) that result in injury to the mother or baby. The likelihood of having a caesarean is increased. Mothers and babies may have complications related to managing blood glucose levels. The baby is more likely to become overweight and develop type 2 diabetes. We wanted to find out the best type of insulin and regimen to use during pregnancy. What evidence did we find? We found five randomised trials (N = 554 women and 554 babies) in October 2016. Each trial looked at different insulin types and ways of giving the insulin. Different outcomes were looked at in each trial. One trial did not include any of the review's main outcomes. All five trials were small, and at a high or unclear risk of bias because of limitations in how the trials were conducted. The quality of the evidence was very low. When rapid-acting human insulin (Lispro) was compared to regular insulin (N = 33), investigators found no clear differences between the groups for pre-eclampsia, abnormalities in the baby, or the need for a caesarean. Macrosomia, perinatal death, birth trauma including shoulder dystocia, nerve palsy, and fracture, and the composite measure of neonatal morbidity were not reported. One trial (N = 43) that compared human insulin to animal insulin did not show any clear difference in the number of babies with macrosomia. Perinatal death, pre-eclampsia, caesarean section, fetal anomaly, birth trauma including shoulder dystocia, nerve palsy, and fracture, and the composite measure of neonatal morbidity were not reported. One trial (N = 93) found no clear differences between pre-mixed and self-mixed insulin groups in the number of babies with macrosomia, and the number of women who had a caesarean section. This trial also compared insulin injected with a pen and a needle (syringe). Women in the insulin pen group were less likely to have a caesarean section, although the number of macrosomic babies was not clearly different. Perinatal death, pre-eclampsia, fetal anomaly, birth trauma including shoulder dystocia, nerve palsy, and fracture, and the composite measure of neonatal morbidity were not reported. One trial (N = 223) comparing insulin Aspart to human insulin did not include any of the review's primary outcomes (macrosomia, perinatal death, pre-eclampsia, caesarean section, fetal anomaly, birth trauma including shoulder dystocia, nerve palsy, and fracture, or the composite measure of neonatal morbidity). One trial (N = 162), which compared long-acting insulin Detemir with the intermediate-acting neutral protamine Hagedorn (NPH) insulin found the number of fetal abnormalities was not clearly different between groups. The trial did not measure macrosomia, perinatal death, pre-eclampsia, caesarean section, birth trauma including shoulder dystocia, nerve palsy, and fracture, or the composite outcome measure of neonatal morbidity. What does this mean? The trials did not provide sufficient evidence to identify clear differences between the various insulin types and regimens. Each study looked at a different type of insulin or regimen, so we could not combine the results. The studies were small, with overall high risk of bias. Therefore, we could not conclude which insulin type or regimen was best for pregnant women with pre-existing diabetes. More research is needed with larger groups of women, better reporting of how the trials were conducted, and more reported outcomes.

Raman P, Shepherd E, Dowswell T, Middleton P, Crowther CA. Different methods and settings for glucose monitoring for gestational diabetes during pregnancy. Cochrane Database of Systematic Reviews 2017;10: - Background Incidence of gestational diabetes mellitus (GDM) is increasing worldwide. Blood glucose monitoring plays a crucial part in maintaining glycaemic control in women with GDM and is generally recommended by healthcare professionals. There are several different methods for monitoring blood glucose which can be carried out in different settings (e.g. at home versus in hospital). Objectives The objective of this review is to compare the effects of different methods and settings for glucose monitoring for women with GDM on maternal and fetal, neonatal, child and adult outcomes, and use and costs of health care. Search methods We searched the Cochrane Pregnancy and Childbirth Group Trials Register (30 September 2016) and
reference lists of retrieved studies. Selection criteria Randomised controlled trials (RCTs) or quasi-randomised controlled trials (qRCTs) comparing different methods (such as timings and frequencies) or settings, or both, for blood glucose monitoring for women with GDM. Data collection and analysis Two authors independently assessed study eligibility, risk of bias, and extracted data. Data were checked for accuracy. We assessed the quality of the evidence for the main comparisons using GRADE, for: - primary outcomes for mothers: that is, hypertensive disorders of pregnancy; caesarean section; type 2 diabetes; and - primary outcomes for children: that is, large-for-gestational age; perinatal mortality; death or serious morbidity composite; childhood/adulthood neurosensory disability; - secondary outcomes for mothers: that is, induction of labour; perinatal trauma; postnatal depression; postnatal weight retention or return to pre-pregnancy weight; and - secondary outcomes for children: that is, neonatal hypoglycaemia; childhood/adulthood adiposity; childhood/adulthood type 2 diabetes. Main results We included 11 RCTs (10 RCTs; one qRCT) that randomised 1272 women with GDM in upper-middle or high-income countries; we considered these to be at a moderate to high risk of bias. We assessed the RCTs under five comparisons. For outcomes assessed using GRADE, we downgraded for study design limitations, imprecision and inconsistency. Three trials received some support from commercial partners who provided glucose meters or financial support, or both. Main comparisons Telemedicine versus standard care for glucose monitoring (five RCTs): we observed no clear differences between the telemedicine and standard care groups for the mother, for: - pre-eclampsia (RR 1.49, 95% confidence interval (CI) 0.69 to 3.20; 275 participants; four RCTs; very low quality evidence); - caesarean section (average RR 1.05, 95% CI 0.72 to 1.53; 478 participants; 5 RCTs; very low quality evidence); and - induction of labour (RR 1.06, 95% CI 0.63 to 1.77; 47 participants; 1 RCT; very low quality evidence); or for the child, for: - large-for-gestational age (RR 1.41, 95% CI 0.76 to 2.64; 228 participants; 3 RCTs; very low quality evidence); - death or serious morbidity composite (RR 1.06, 95% CI 0.68 to 1.66; 57 participants; 1 RCT; very low quality evidence); and - neonatal hypoglycaemia (RR 1.14, 95% CI 0.48 to 2.72; 198 participants; 3 RCTs; very low quality evidence). There were no perinatal deaths in two RCTs (131 participants; very low quality evidence). Self-monitoring versus periodic glucose monitoring (two RCTs): we observed no clear differences between the self-monitoring and periodic glucose monitoring groups for the mother, for: - pre-eclampsia (RR 0.17, 95% CI 0.01 to 3.49; 58 participants; 1 RCT; very low quality evidence) and - caesarean section (average RR 1.18, 95% CI 0.61 to 2.27; 400 participants; 2 RCTs; low quality evidence); or for the child, for: - perinatal mortality (RR 1.54, 95% CI 0.21 to 11.24; 400 participants; 2 RCTs; very low quality evidence); - large-for-gestational age (RR 0.82, 95% CI 0.50 to 1.37; 400 participants; 2 RCTs; low quality evidence); and - neonatal hypoglycaemia (RR 0.64, 95% CI 0.39 to 1.06; 391 participants; 2 RCTs; low quality evidence). Continuous glucose monitoring system (CGMS) versus self-monitoring of glucose (two RCTs): we observed no clear differences between the CGMS and self-monitoring groups for the mother, for: - caesarean section (RR 0.91, 95% CI 0.68 to 1.20; 179 participants; 2 RCTs; very low quality evidence); or for the child, for: - large-for-gestational age (RR 0.67, 95% CI 0.43 to 1.05; 106 participants; 1 RCT; very low quality evidence) and - neonatal hypoglycaemia (RR 0.79, 95% CI 0.35 to 1.78; 179 participants; 2 RCTs; very low quality evidence). There were no perinatal deaths in the two RCTs (179 participants; very low quality evidence). Other comparisons Modem versus telephone transmission for glucose monitoring (one RCT): none of the review’s primary outcomes were reported in this trial Postprandial versus preprandial glucose monitoring (one RCT): we observed no clear differences between the postprandial and preprandial glucose monitoring groups for the mother, for: - pre-eclampsia (RR 1.00, 95% CI 0.15 to 6.68; 66 participants; 1 RCT); - caesarean section (RR 0.62, 95% CI 0.29 to 1.29; 66 participants; 1 RCT); and - perinatal trauma (RR 0.39, 95% CI 0.11 to 1.32; 58 participants; 1 RCT); or for the child, for: - neonatal hypoglycaemia (RR 0.14, 95% CI 0.02 to 1.10; 66 participants; 1 RCT). There were fewer large-for-gestational-age infants born to mothers in the postprandial compared with the preprandial glucose monitoring group (RR 0.29, 95% CI 0.11 to 0.78; 66 participants; 1 RCT). Authors’ conclusions Evidence from 11 RCTs assessing different methods or settings for glucose monitoring for GDM suggests no clear differences for the primary outcomes or other secondary outcomes assessed in this review. However, current evidence is limited by the small number of RCTs for the comparisons assessed, small sample sizes, and the variable methodological quality of the RCTs. More evidence is needed to assess the effects of different methods and settings for glucose monitoring for GDM on outcomes for mothers and their children, including use and costs of health care. Future RCTs may consider collecting and reporting on the standard outcomes suggested in this review. Plain language summary Different methods and settings for glucose monitoring for women with gestational diabetes during pregnancy What is the issue? Gestational diabetes mellitus (GDM) is a glucose intolerance leading to high concentrations of glucose (sugar) in the blood (hyperglycaemia) that begins or is first recognised during pregnancy. Monitoring of blood glucose levels is an important way to maintain control of sugar concentrations in the blood. There are several different methods for monitoring blood glucose which can be carried out in different settings (e.g. at home or hospital), however it is not clear which is best for limiting health complications for women and their babies. Why is this important? Women with GDM are more likely to develop pre-eclampsia (a dangerous condition characterised by high blood pressure)
during pregnancy, and to have the birth induced, suffer trauma to the perineum during birth, or to give birth by caesarean section. Their babies are more likely to be large for their gestational age at birth, develop low blood sugar (hypoglycaemia), and suffer from complications leading to death. Both the women and their babies are more likely to develop long-term health complications, including type 2 diabetes. What evidence did we find? We searched the medical literature in September 2016 and included 11 randomised controlled trials (RCTs) involving 1272 women with GDM and their babies. Three trials were supported by commercial partners. We included five different comparisons: 1) telemedicine (transmission of glucose concentrations from home to healthcare professionals for review) versus standard care (face-to-face review in a clinic/hospital) (five RCTs); 2) self-monitoring of glucose (at home) versus periodic monitoring of glucose (less frequently at face-to-face visits) (two RCTs); 3) use of a continuous glucose monitoring system (CGMS) versus less frequent self-monitoring of glucose (two RCTs); 4) modern technology (transmitting glucose concentrations directly from glucose meters to healthcare professionals) versus telephone transmission of glucose concentrations (one RCT); 5) postprandial (after meal) versus preprandial (before meal) monitoring of glucose (one RCT). Telemedicine versus standard care for glucose monitoring (five RCTs): there were no clear differences between women in the telemedicine and standard care groups for pre-eclampsia or hypertension, caesarean section or induction of labour; or for their babies being born large-for-gestational age, developing a serious morbidity, or having hypoglycaemia. There were no deaths in the two RCTs that reported on deaths of babies. Self-monitoring versus periodic glucose monitoring (two RCTs): there were no clear differences between women in the self-monitoring and periodic glucose monitoring groups for pre-eclampsia or caesarean section; or for their babies dying, being born large-for-gestational age, or developing hypoglycaemia. CGMS versus self-monitoring of glucose (two RCTs): there was no clear difference between women in the CGMS and self-monitoring groups for caesarean section; or for babies being born large-for-gestational age, or developing hypoglycaemia. There were no deaths of babies in the two RCTs. Modern versus telephone transmission for glucose monitoring (one RCT): this RCT reported none of the outcomes we considered most important. Postprandial versus preprandial glucose monitoring (one RCT): there were no clear differences between women in the postprandial and preprandial glucose monitoring groups for pre-eclampsia, caesarean section or perineal trauma; or for babies developing hypoglycaemia. Babies born to women in the postprandial glucose monitoring group were less likely to be born large-for-gestational age than babies in the preprandial group. The quality of the evidence for the above findings was low or very low. None of the 11 RCTs reported on postnatal depression, postnatal weight retention, return to pre-pregnancy weight, or development of type 2 diabetes for the women; or disability, adiposity or development of type 2 diabetes for the babies as children or adults. What does this mean? Blood glucose monitoring is an important strategy for managing GDM, however it remains unclear what methods are best. Conclusive evidence from RCTs is not yet available to guide practice, although a range of methods has been investigated. Few RCTs have compared the same or similar interventions, RCTs have been small and have reported limited findings. Further large, well-designed, RCTs are required to assess the effects of different methods and settings for blood glucose monitoring for women with GDM in order to improve outcomes for women and their babies in the short and long term.

Shepherd E, Gomersall JC, Tieu J, Han S, Crowther CA, Middleton P. Combined diet and exercise interventions for preventing gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2017;11):
primary review outcomes, there was a possible reduced risk of GDM in the diet and exercise intervention group compared with the standard care group (average risk ratio (RR) 0.85, 95% confidence interval (CI) 0.71 to 1.01; 6633 women; 19 RCTs; Tau² = 0.05; I² = 42%; P = 0.07; moderate-quality evidence). There was also a possible reduced risk of caesarean section (RR 0.95, 95% CI 0.88 to 1.02; 6089 women; 14 RCTs; moderate-quality evidence). No clear differences were seen between groups for pre-eclampsia (RR 0.98, 95% CI 0.79 to 1.22; 5368 participants; 8 RCTs; low-quality evidence), pregnancy-induced hypertension and/or hypertension (average RR 0.78, 95% CI 0.47 to 1.27; 3073 participants; 6 RCTs; Tau² = 0.19; I² = 62%; very low-quality evidence), perinatal mortality (RR 0.82, 95% CI 0.42 to 1.63; 3757 participants; 2 RCTs; low-quality evidence) or large-for-gestational age (RR 0.93, 95% CI 0.81 to 1.07; 5353 participants; 11 RCTs; low-quality evidence). No data were reported for infant mortality or morbidity composite. Subgroup analyses (based on trial design, maternal body mass index (BMI) and ethnicity) revealed no clear differential treatment effects. We were unable to assess the impact of maternal age, parity and specific features of the diet and exercise interventions. Findings from sensitivity analyses (based on RCT quality) generally supported those observed in the main analyses. We were not able to perform subgroup analyses based on maternal age, parity or nature of the exercise/dietary interventions due to the paucity of information/data on these characteristics and the inability to meaningfully group intervention characteristics. For most of the secondary review outcomes assessed using GRADE, there were no clear differences between groups, including for perinatal trauma (RR 1.27, 95% CI 0.78 to 2.05; 2733 participants; 2 RCTs; moderate-quality evidence), neonatal hypoglycaemia (average RR 1.42, 95% CI 0.67 to 2.98; 3653 participants; 2 RCTs; Tau² = 0.23 I² = 77%; low quality evidence); and childhood adiposity (BMI z score) (MD 0.05, 95% CI -0.29 to 0.40; 794 participants; 2 RCTs; Tau² = 0.04; I² = 59%; low-quality evidence). However, there was evidence of less gestational weight gain in the diet and exercise intervention group compared with the control group (mean difference (MD) -0.89 kg, 95% CI -1.39 to -0.40; 5052 women; 16 RCTs; Tau² = 0.37; I² = 43%; moderate-quality evidence). No data were reported for maternal postnatal depression or type 2 diabetes; childhood/adulthood type 2 diabetes, or neurosensory disability. Authors' conclusions Moderate-quality evidence suggests reduced risks of GDM and caesarean section with combined diet and exercise interventions during pregnancy as well as reductions in gestational weight gain, compared with standard care. There were no clear differences in hypertensive disorders of pregnancy, perinatal mortality, large-for-gestational age, perinatal trauma, neonatal hypoglycaemia and childhood adiposity (moderate- to very low-quality evidence). Using GRADE methodology, the evidence was assessed as moderate to very low quality. Downgrading decisions were predominantly due to design limitations (risk of bias), and imprecision (uncertain effect estimates, and at times, small sample sizes and low event rates), however two outcomes (pregnancy-induced hypertension/hypertension and neonatal hypoglycaemia), were also downgraded for unexplained inconsistency (statistical heterogeneity). Due to the variability of the diet and exercise components tested in the included studies, the evidence in this review has limited ability to inform practice. Future studies could describe the interventions used in more detail, if and how these influenced behaviour change and ideally be standardised between studies. Studies could also consider using existing core outcome sets to facilitate more standardised reporting. Plain language summary Combined diet and exercise in pregnancy for preventing gestational diabetes mellitus Review question What are the effects of combined diet and exercise for preventing gestational diabetes mellitus (GDM), and related health problems for mothers and their babies? This is an update of a Cochrane review that was first published in 2015. Background GDM is high blood sugar (hyperglycaemia) during pregnancy. Up to a quarter of pregnant women develop GDM, with some at a higher risk than others (such as overweight or obese women, older women, and those of particular ethnicities). GDM can lead to significant health problems for women and their babies. In the short term, women with GDM may develop pre-eclampsia (high blood pressure (hypertension) and protein in the urine), or give birth by caesarean section. Their babies may grow large for their gestational age, and, as a result, be injured at birth, and/or cause injury to their mothers during birth. Babies of mothers with GDM often have low blood glucose (hypoglycaemia) and are overweight. Later in life, health problems such as neurosensory disabilities and type 2 diabetes can develop in these babies. Eating well and exercising is known to prevent type 2 diabetes and may be effective for preventing GDM. Study characteristics We searched for evidence in November 2016 and included 23 randomised controlled trials (RCTs) (involving 8918 women and their 8709 babies). Most studies were undertaken in high-income countries. All of the studies compared women receiving diet and exercise programs with women receiving standard care without diet and exercise programs. The studies varied in the diet and exercise programs evaluated and health outcomes reported. None reported receiving funding from a drug manufacturer or agency with interests in the results. Key results Findings from 19 studies (6633 women) showed a possible reduction in GDM in women who received diet and exercise programs compared with women who received standard care. Fourteen studies (6089 women) showed a possible reduction in caesarean birth (14 studies; 6089 women) and 16 studies (5052 women) showed lower weight gain during pregnancy in women who received exercise programs. We found no differences between groups in other health problems for: pre-eclampsia (8 studies; 5366 women); high blood pressure (6 studies; 3073 women); a
large for age baby at birth (11 studies; 5353 babies); and perineal trauma (2 studies; 2733 women). Death of babies around birth (2 studies; 3757 babies), the baby having low blood glucose after birth (2 studies; 3653 babies), and infants being overweight (2 studies; 794 infants) did not differ in the two groups. Effects on depression or type 2 diabetes for mothers, a combined outcome of death or ill-health for babies, or type 2 diabetes or neurosensory disability for babies as children were not reported. Participant views of programs were examined. The evidence suggests combined diet and exercise programs may be effective for preventing GDM though the optimum components of these programs are not yet clear. Future studies could describe the interventions used in more detail, if and how these influenced behaviour change and ideally be standardised between studies. Studies could also consider measuring similar maternal and infant outcomes and report them in a standardised way. Quality of the evidence The overall risk of bias was judged unclear due to lack of information on methods. We assessed evidence quality using GRADE considerations for selected key outcomes. Our assessments ranged from moderate to very low.

Tieu J, Shepherd E, Middleton P, Crowther CA. Interconception care for women with a history of gestational diabetes for improving maternal and infant outcomes. Cochrane Database of Systematic Reviews 2017;8(CD010211

BACKGROUND: Gestational diabetes mellitus (GDM) is associated with adverse health outcomes for mothers and their infants both perinatally and long term. Women with a history of GDM are at risk of recurrence in subsequent pregnancies and may benefit from intervention in the interconception period to improve maternal and infant health outcomes.

OBJECTIVES: To assess the effects of interconception care for women with a history of GDM on maternal and infant health outcomes.

SEARCH METHODS: We searched Cochrane Pregnancy and Childbirth's Trials Register (7 April 2017) and reference lists of retrieved studies.

SELECTION CRITERIA: Randomised controlled trials, including quasi-randomised controlled trials and cluster-randomised trials evaluating any protocol of interconception care with standard care or other forms of interconception care for women with a history of GDM on maternal and infant health outcomes.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed study eligibility. In future updates of this review, at least two review authors will extract data and assess the risk of bias of included studies; the quality of the evidence will be assessed using the GRADE approach.

MAIN RESULTS: No eligible published trials were identified. We identified a completed randomised controlled trial that was designed to evaluate the effects of a diet and exercise intervention compared with standard care in women with a history of GDM, however to date, it has only published results on women who were pregnant at randomisation (and not women in the interconception period). We also identified an ongoing trial, in obese women with a history of GDM planning a subsequent pregnancy, which is assessing the effects of an intensive lifestyle intervention, supported with liraglutide treatment, compared with usual care. We also identified a trial that was designed to evaluate the effects of a weight loss and exercise intervention compared with lifestyle education also in obese women with a history of GDM planning a subsequent pregnancy, however it has not yet been published. These trials will be re-considered for inclusion in the next review update.

AUTHORS' CONCLUSIONS: The role of interconception care for women with a history of GDM remains unclear. Randomised controlled trials are required evaluating different forms and protocols of interconception care for these women on perinatal and long-term maternal and infant health outcomes, acceptability of such interventions and cost-effectiveness.

Tieu J, Coat S, Hague W, Middleton P, Shepherd E. Oral anti-diabetic agents for women with established diabetes/impaired glucose tolerance or previous gestational diabetes planning pregnancy, or pregnant women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2017;10):

- Background While most guidance recommends the use of insulin in women whose pregnancies are affected by pre-existing diabetes, oral anti-diabetic agents may be more acceptable to women. The effects of these oral anti-diabetic agents on maternal and infant health outcomes need to be established in pregnant women with pre-existing diabetes or impaired glucose tolerance, as well as in women with previous gestational diabetes mellitus preconceptionally or during a subsequent pregnancy. This review is an update of a review that was first published in 2010. Objectives To investigate the effects of oral anti-diabetic agents in women with established diabetes, impaired glucose tolerance or previous gestational diabetes who are planning a pregnancy, or pregnant women with pre-existing diabetes, on maternal and infant health. The use of oral anti-diabetic agents for the management of gestational diabetes in a current pregnancy is evaluated in a separate Cochrane Review. Search methods We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 October 2016) and reference lists of retrieved studies. Selection criteria Randomised controlled
trials (RCTs) and quasi-RCTs assessing the effects of oral anti-diabetic agents in women with established diabetes, impaired glucose tolerance or previous gestational diabetes who were planning a pregnancy, or pregnant women with pre-existing diabetes. Cluster-RCTs were eligible for inclusion, but none were identified.

Data collection and analysis Two review authors independently assessed study eligibility, extracted data and assessed the risk of bias of the included RCTs. Review authors checked the data for accuracy, and assessed the quality of the evidence using the GRADE approach. Main results We identified six RCTs (707 women), eligible for inclusion in this updated review; however, three RCTs had mixed populations (that is, they included pregnant women with gestational diabetes) and did not report data separately for the relevant subset of women for this review. Therefore we have only included outcome data from three RCTs; data were available for 241 women and their infants. The three RCTs all compared an oral anti-diabetic agent (metformin) with insulin. The women in the RCTs that contributed data had type 2 diabetes diagnosed before or during their pregnancy. Overall, the RCTs were judged to be at varying risk of bias. We assessed the quality of the evidence for selected important outcomes using GRADE; the evidence was low- or very low-quality, due to downgrading because of design limitations (risk of bias) and imprecise effect estimates (for many outcomes only one or two RCTs contributed data). For our primary outcomes there was no clear difference between metformin and insulin groups for pre-eclampsia (risk ratio (RR) 0.63, 95% confidence interval (CI) 0.33 to 1.20; RCTs = 2; participants = 227; very low-quality evidence) although in one RCT women receiving metformin were less likely to have pregnancy-induced hypertension (RR 0.58, 95% CI 0.37 to 0.91; RCTs = 1; participants = 206; low-quality evidence). Women receiving metformin were less likely to have a caesarean section compared with those receiving insulin (RR 0.73, 95% CI 0.61 to 0.88; RCTs = 3; participants = 241; low-quality evidence). In one RCT there was no clear difference between groups for large-for-gestational-age infants (RR 1.12, 95% CI 0.73 to 1.72; RCTs = 1; participants = 206; very low-quality evidence). There were no perinatal deaths in two RCTs (very low-quality evidence). Neonatal mortality or morbidity composite outcome and childhood/adulthood neurosensory disability were not reported. For other secondary outcomes we assessed using GRADE, there were no clear differences between metformin and insulin groups for induction of labour (RR 1.42, 95% CI 0.62 to 3.28; RCTs = 2; participants = 35; very low-quality evidence), though infant hypoglycaemia was reduced in the metformin group (RR 0.34, 95% CI 0.18 to 0.62; RCTs = 3; infants = 41; very low-quality evidence). Perineal trauma, maternal postnatal depression and postnatal weight retention, and childhood/adulthood adiposity and diabetes were not reported. Authors’ conclusions There are insufficient RCT data to evaluate the use of oral anti-diabetic agents in women with established diabetes, impaired glucose tolerance or previous gestational diabetes who are planning a pregnancy, or in pregnant women with pre-existing diabetes. Low to very low-quality evidence suggests possible reductions in pregnancy-induced hypertension, caesarean section birth and neonatal hypoglycaemia with metformin compared with insulin for women with type 2 diabetes diagnosed before or during their pregnancy, and no clear differences in pregnancy-induced hypertension, induction of labour and babies that are large-for-gestational age. Further high-quality RCTs that compare any combination of oral anti-diabetic agent, insulin and dietary and lifestyle advice for these women are needed. Future RCTs could be powered to evaluate effects on short- and long-term clinical outcomes; such RCTs could attempt to collect and report on the standard outcomes suggested in this review. We have identified three ongoing studies and four are awaiting classification. We will consider these when this review is updated. Plain language summary Oral anti-diabetic agents for women with diabetes or previous diabetes planning a pregnancy, or pregnant women with pre-existing diabetes What is the issue? Pre-existing diabetes and gestational diabetes can increase the risks of a number of poor outcomes for both mothers and their babies. For the mother, these include pregnancy-induced high blood pressure (pre-eclampsia) with additional fluid retention and protein in the urine; and giving birth by caesarean. For the infant, these can include preterm birth; as well as an increased risk of the presence of physical defects at birth such as heart defects, brain, spine, and spinal cord defects, Down syndrome; and spontaneous abortion. Other complications at birth include babies that are large for their gestational age, and obstructed labour (shoulder dystocia) caused by one of the shoulders becoming stuck in the birth canal once the baby’s head has been born. Why is this important? Being pregnant can trigger diabetes (gestational diabetes) in women with impaired glucose tolerance. Women who have had gestational diabetes are at risk of developing diabetes later in life. This means that management is important for women with impaired glucose tolerance or previous gestational diabetes, as well as for women with established diabetes. Women with established diabetes need good blood sugar control before they become pregnant. Insulin gives good blood sugar control and does not affect the development of the baby, but women may find oral anti-diabetic agents more convenient and acceptable than insulin injections. However little is known about the effects of these oral agents. This review sought to investigate the effects of oral anti-diabetic agents in women with established diabetes, impaired glucose tolerance or previous gestational diabetes who were planning a pregnancy, or pregnant women with pre-existing diabetes, on maternal and infant health. This review is an update of a review that was first published in 2010. What evidence did we find? We searched for evidence from randomised controlled trials (RCTs) on 31 October 2016 and included six RCTs (707 women).
Three RCTs included women with current gestational diabetes and did not report data separately for the population of women relevant to this review. Therefore we have only included outcome data from three RCTs, involving 241 pregnant women and their infants. The quality of the evidence was assessed as being low or very low and the overall risk of bias of the RCTs was varied. The three RCTs all compared an oral anti-diabetic agent (metformin) with insulin in pregnant women with pre-existing (type 2) diabetes. There was no clear difference in the development of pre-eclampsia (high blood pressure and protein in the urine) for women who received metformin compared with insulin (2 RCTs; 227 women; very low-quality evidence), though women receiving metformin were less likely to have pregnancy-induced high blood pressure in one RCT (206 women; low-quality evidence). Women who received metformin were less likely to have a caesarean section birth (3 RCTs; 241 women; low-quality evidence), though no difference was observed in induction of labour (2 RCTs; 35 women; very low-quality evidence). There was no clear difference between groups of infants born to mothers who received metformin or insulin for being large-for-gestational age (1 RCT; 206 infants; very low-quality evidence), though infants born to mothers who received metformin were less likely to have low blood sugar (hypoglycaemia) (3 RCTs; 241 infants; very low-quality evidence). There were no infant deaths (before birth or shortly afterwards) (2 RCTs; very low-quality evidence). The RCTs did not report on many important short- and long-term outcomes, including perineal trauma and a combined outcome of infant death or morbidity, postnatal depression and weight retention for mothers, and adiposity or disability in childhood or adulthood for infants. What does this mean? There is not enough evidence to guide us on the effects of oral anti-diabetic agents in women with established diabetes, impaired glucose tolerance or previous gestational diabetes who are planning a pregnancy, or pregnant women with pre-existing diabetes. Further large, well-designed, RCTs are required and could assess and report on the outcomes suggested in this review, including both short- and long-term outcomes for mothers and their infants.


- Background Gestational diabetes mellitus (GDM) is a form of diabetes that occurs in pregnancy. Although GDM usually resolves following birth, it is associated with significant morbidities for mothers and their infants in the short and long term. There is strong evidence to support treatment for GDM. However, there is uncertainty as to whether or not screening all pregnant women for GDM will improve maternal and infant health and if so, the most appropriate setting for screening. This review updates a Cochrane Review, first published in 2010, and subsequently updated in 2014. Objectives To assess the effects of screening for gestational diabetes mellitus based on different risk profiles and settings on maternal and infant outcomes. Search methods We searched Cochrane Pregnancy and Childhood's Trials Register (31 January 2017), ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) (14 June 2017), and reference lists of retrieved studies. Selection criteria We included randomised and quasi-randomised trials evaluating the effects of different protocols, guidelines or programmes for screening for GDM based on different risk profiles and settings, compared with the absence of screening, or compared with other protocols, guidelines or programmes for screening. We planned to include trials published as abstracts only and cluster-randomised trials, but we did not identify any. Cross-over trials are not eligible for inclusion in this review. Data collection and analysis Two review authors independently assessed study eligibility, extracted data and assessed the risk of bias of the included trials. We resolved disagreements through discussion or through consulting a third reviewer. Main results We included two trials that randomised 4523 women and their infants. Both trials were conducted in Ireland. One trial (which quasi-randomised 3742 women, and analysed 3152 women) compared universal screening versus risk factor-based screening, and one trial (which randomised 781 women, and analysed 690 women) compared primary care screening versus secondary care screening. We were not able to perform meta-analyses due to the different interventions and comparisons assessed. Overall, there was moderate to high risk of bias due to one trial being quasi-randomised, inadequate blinding, and incomplete outcome data in both trials. We used GRADEpro GDT software to assess the quality of the evidence for selected outcomes for the mother and her child. Evidence was downgraded for study design limitations and imprecision of effect estimates. Universal screening versus risk-factor screening (one trial) Mother More women were diagnosed with GDM in the universal screening group than in the risk-factor screening group (risk ratio (RR) 1.85, 95% confidence interval (CI) 1.12 to 3.04; participants = 3152; low-quality evidence). There were no data reported under this comparison for other maternal outcomes including hypertensive disorders of pregnancy, caesarean birth, perineal trauma, gestational weight gain, postnatal depression, and type 2 diabetes. Child Neonatal outcomes: long-for-gestational age, perinatal mortality, mortality or morbidity composite, hypoglycaemia; and childhood/adulthood outcomes: adiposity, type 2 diabetes, and neurosensory disability, were not reported under this comparison. Primary care screening versus secondary care screening (one trial) Mother There was no clear difference between the primary care and secondary care screening groups for GDM (RR 0.91, 95% CI 0.50 to 1.66;
participants = 690; low-quality evidence), hypertension (RR 1.41, 95% CI 0.77 to 2.59; participants = 690; low-quality evidence), pre-eclampsia (RR 0.80, 95% CI 0.36 to 1.78; participants = 690; low-quality evidence), or caesarean section birth (RR 1.00, 95% CI 0.80 to 1.27; participants = 690; low-quality evidence). There were no data reported for perineal trauma, gestational weight gain, postnatal depression, or type 2 diabetes. Child There was no clear difference between the primary care and secondary care screening groups for large-for-gestational age (RR 1.37, 95% CI 0.96 to 1.96; participants = 690; low-quality evidence), neonatal complications: composite outcome, including: hypoglycaemia, respiratory distress, need for phototherapy, birth trauma, shoulder dystocia, five minute Apgar less than seven at one or five minutes, prematurity (RR 0.99, 95% CI 0.57 to 1.71; participants = 690; low-quality evidence), or neonatal hypoglycaemia (RR 1.10, 95% CI 0.28 to 4.38; participants = 690; very low-quality evidence). There was one perinatal death in the primary care screening group and two in the secondary care screening group (RR 1.10, 95% CI 0.10 to 12.12; participants = 690; very low-quality evidence). There were no data for neurosensory disability, or childhood/adulthood adiposity or type 2 diabetes. Authors' conclusions There are insufficient randomised controlled trial data evaluating the effects of screening for GDM based on different risk profiles and settings on maternal and infant outcomes. Low-quality evidence suggests universal screening compared with risk factor-based screening leads to more women being diagnosed with GDM. Low to very low-quality evidence suggests no clear differences between primary care and secondary care screening, for outcomes: GDM, hypertension, pre-eclampsia, caesarean birth, large-for-gestational age, neonatal complications composite, and hypoglycaemia. Further, high-quality randomised controlled trials are needed to assess the value of screening for GDM, which may compare different protocols, guidelines or programmes for screening (based on different risk profiles and settings), with the absence of screening, or with other protocols, guidelines or programmes. There is a need for future trials to be sufficiently powered to detect important differences in short- and long-term maternal and infant outcomes, such as those important outcomes pre-specified in this review. As only a proportion of women will be diagnosed with GDM in these trials, large sample sizes may be required. Plain language summary Screening women for gestational diabetes in pregnancy based on whether they are considered at risk, and in different settings What is the issue? What are the effects of screening all women for gestational diabetes mellitus (GDM), compared with only screening those who are 'at risk'? What are the effects of screening women for GDM in different settings (such as in the community versus the hospital)? This review updates a Cochrane Review, first published in 2010, and subsequently updated in 2014. Why is this important? GDM is a form of diabetes that can develop during pregnancy, and can increase the risk of complications for mothers and their babies. Women with GDM are more likely to develop pre-eclampsia (high blood pressure and protein in the urine) and require a caesarean section. For babies, potential problems include being large for gestational age (growing larger than they normally would), or having hypoglycaemia (low blood sugar) after birth. Although GDM usually resolves following birth, mothers and their babies are at risk of developing type 2 diabetes in the future. Treating GDM can improve health outcomes. Women often do not know they have GDM. Screening to identify and treat GDM in pregnant women may therefore improve outcomes. The two main approaches are 'universal' where all women undergo screening; and 'selective' or 'risk factor'-based where only those women 'at risk' are screened. The risk factors for GDM include certain ethnicities, being older, overweight or obese, having had a previous large baby, or a family history of GDM or type 2 diabetes. It is possible to screen for GDM in different settings, such as in the community (e.g. a general practice clinic) or in hospital. The ideal screening method for GDM that leads to the best health outcomes for mothers and their baby remains unclear. What evidence did we find? We searched for evidence (January 2017) and included two trials involving 4523 women and their babies. Both trials were conducted in Ireland and were at a moderate to high risk of bias. We could not combine the data from these trials because they looked at different interventions and comparisons. One compared 'universal' screening with 'risk factor'-based screening for GDM. The other compared screening women at their general practitioners' clinic (primary care) versus at the hospital (secondary care). In one trial (with information available for 3152 women), more women were diagnosed with GDM in the group of women who received 'universal' screening, compared with the group of women with 'risk factor'-based screening (low-quality evidence). The trial did not report on outcomes relating to the mothers, including high blood pressure disorders of pregnancy, caesarean birth, perineal trauma, weight gain in pregnancy, postnatal depression, and type 2 diabetes. The trial did not report outcomes relating to the babies including being born large-for-gestational age, death (before or shortly after birth), death or a serious complication, hypoglycaemia, or adiposity, type 2 diabetes, and disability in childhood or adulthood. In the second trial (with information available for 690 women), screening at the general practitioner's clinic versus the hospital did not make a clear difference to the number of women diagnosed with GDM (low-quality evidence), high blood pressure (1 ow-quality evidence), pre-eclampsia (low-quality evidence), or the number who had a caesarean birth (1 ow-quality evidence). This trial did not report perineal trauma, weight gain in pregnancy, postnatal depression, or type 2 diabetes. Screening at the general practitioner's clinic versus at the hospital did not make a clear difference to the number of babies born large-for-gestational age (1 ow-quality evidence), death (before or
shortly after birth), death or a serious complication (low-quality evidence), or hypoglycaemia (very low-quality evidence). Childhood or adulthood adiposity, type 2 diabetes, and disability were not reported in the trial. What does this mean? There is not enough evidence to guide us on effects of screening for GDM based on different risk profiles or settings on outcomes for women and their babies. Further large, well-designed, randomised controlled trials are required to assess important short- and long-term outcomes for mothers and their babies.


- Background Gestational diabetes mellitus (GDM) is a form of diabetes occurring during pregnancy which can result in short- and long-term adverse outcomes for women and babies. With an increasing prevalence worldwide, there is a need to assess strategies, including dietary advice interventions, that might prevent GDM. Objectives To assess the effects of dietary advice interventions for preventing GDM and associated adverse health outcomes for women and their babies. Search methods We searched Cochrane Pregnancy and Childbirth's Trials Register (3 January 2016) and reference lists of retrieved studies. Selection criteria Randomised controlled trials (RCTs) and quasi-RCTs assessing the effects of dietary advice interventions compared with no intervention (standard care), or to different dietary advice interventions. Cluster-RCTs were eligible for inclusion but none were identified. Data collection and analysis Two review authors independently assessed study eligibility, extracted data and assessed the risk of bias of the included studies. Data were checked for accuracy. The quality of the evidence was assessed using the GRADE approach. Main results We included 11 trials involving 2786 women and their babies, with an overall unclear to moderate risk of bias. Six trials compared dietary advice interventions with standard care; four compared low glycaemic index (GI) with moderate- to high-GI dietary advice; one compared specific (high-fibre focused) with standard dietary advice. Dietary advice interventions versus standard care (six trials) Considering primary outcomes, a trend towards a reduction in GDM was observed for women receiving dietary advice compared with standard care (average risk ratio (RR) 0.60, 95% confidence interval (CI) 0.35 to 1.04; five trials, 1279 women; Tau² = 0.20; I² = 56%; P = 0.07; GRADE: very low-quality evidence ); subgroup analysis suggested a greater treatment effect for overweight and obese women receiving dietary advice. While no clear difference was observed for pre-eclampsia (RR 0.61, 95% CI 0.25 to 1.46; two trials, 282 women; GRADE: low-quality evidence ) a reduction in pregnancy-induced hypertension was observed for women receiving dietary advice (RR 0.30, 95% CI 0.10 to 0.88; two trials, 282 women; GRADE: low-quality evidence ). One trial reported on perinatal mortality, and no deaths were observed (GRADE: very low-quality evidence ). None of the trials reported on large-for-gestational age or neonatal mortality and morbidity. For secondary outcomes, no clear differences were seen for caesarean section (average RR 0.98, 95% CI 0.78 to 1.24; four trials, 1194 women; Tau² = 0.02; I² = 36%; GRADE: low-quality evidence ) or perineal trauma (RR 0.83, 95% CI 0.23 to 3.08; one trial, 759 women; GRADE: very low-quality evidence ). Women who received dietary advice gained less weight during pregnancy (mean difference (MD) -4.70 kg, 95% CI -8.07 to -1.34; five trials, 1336 women; Tau² = 13.64; I² = 96%; GRADE: low-quality evidence ); the result should be interpreted with some caution due to considerable heterogeneity. No clear differences were seen for the majority of secondary outcomes reported, including childhood/adulthood adiposity (skin-fold thickness at six months) (MD -0.10 mm, 95% CI -0.71 to 0.51; one trial, 132 children; GRADE: low-quality evidence ). Women receiving dietary advice had a lower well-being score between 14 and 28 weeks, more weight loss at three months, and were less likely to have glucose intolerance (one trial). The trials did not report on other secondary outcomes, particularly those related to long-term health and health service use and costs. We were not able to assess the following outcomes using GRADE: postnatal depression; maternal type 2 diabetes; neonatal hypoglycaemia; childhood/adulthood type 2 diabetes; and neurosensory disability. Low-GI dietary advice versus moderate- to high-GI dietary advice (four trials) Considering primary outcomes, no clear differences were shown n the risks of GDM (RR 0.91, 95% CI 0.63 to 1.31; four trials, 912 women; GRADE: low-quality evidence ) or large-for-gestational age (average RR 0.80, 95% CI 0.19 to 1.86; three trials, 777 babies; Tau² = 0.61; P = 0.07; I² = 62%; GRADE: very low-quality evidence ) between the low-GI and moderate- to high-GI dietary advice groups. The trials did not report on: hypertensive disorders of pregnancy; perinatal mortality; neonatal mortality and morbidity. No clear differences were shown for caesarean birth (RR 1.27, 95% CI 0.79 to 2.04; two trials, 201 women; GRADE: very low-quality evidence ) and gestational weight gain (MD -1.23 kg, 95% CI -4.08 to 1.61; four trials, 787 women; Tau² = 7.31; I² = 96%; GRADE: very low-quality evidence ), or for other reported secondary outcomes. The trials did not report the majority of secondary outcomes including those related to long-term health and health service use and costs. We were not able to assess the following outcomes using GRADE: perineal trauma; postnatal depression; maternal type 2 diabetes; neonatal hypoglycaemia; childhood/adulthood adiposity; type 2 diabetes; and neurosensory disability. High-fibre dietary advice versus standard dietary advice (one trial) The one trial in this comparison reported on two secondary outcomes. No clear difference between the high-fibre and standard dietary advice groups observed for mean
blood glucose (following an oral glucose tolerance test at 35 weeks), and birthweight. Authors' conclusions
Very low-quality evidence from five trials suggests a possible reduction in GDM risk for women receiving
dietary advice versus standard care, and low-quality evidence from four trials suggests no clear difference for
women receiving low- versus moderate- to high-GI dietary advice. A possible reduction in pregnancy-induced
hypertension for women receiving dietary advice was observed and no clear differences were seen for other
reported primary outcomes. There were few outcome data for secondary outcomes. For outcomes assessed
using GRADE, evidence was considered to be low to very low quality, with downgrading based on study
limitations (risk of bias), imprecision, and inconsistency. More high-quality evidence is needed to determine
the effects of dietary advice interventions in pregnancy. Future trials should be designed to monitor
adherence, women's views and preferences, and powered to evaluate effects on short- and long-term
outcomes; there is a need for such trials to collect and report on core outcomes for GDM research. We have
identified five ongoing studies and four are awaiting classification. We will consider these in the next review
update. Plain language summary Dietary advice during pregnancy to prevent gestational diabetes What is the
issue? Can dietary advice for pregnant women prevent the development of diabetes in pregnancy, known as
gestational diabetes mellitus (GDM), which can cause health complications for women and their babies? Why
is this important? Women with GDM have an increased risk of developing high blood pressure and protein in
their urine during pregnancy (pre-eclampsia), and of having a caesarean section birth. Their babies may grow
large and, as a result, be injured at birth, or cause injury to their mothers during birth. Additionally, there can
be long-term health problems for women and their babies, including an increased risk of cardiovascular
disease or type 2 diabetes. The number of women being diagnosed with GDM is increasing around the world,
so finding simple and cost-effective ways to prevent women developing GDM is important. Carbohydrates are
the main nutrient affecting blood glucose after meals. The glycaemic index (GI) can be used to characterise
the capability of carbohydrate-based foods to raise these levels. Some diets, for example, those with low-fibre
and high-GI foods, can increase the risk of developing GDM. It has been suggested that dietary advice
interventions in pregnancy may help to prevent women developing GDM. What evidence did we find? We
searched for studies on 3 January 2016, and included 11 randomised controlled trials involving 2786 pregnant
women and their babies. The quality of the evidence was assessed as low or very low and the overall risk of
bias of the trials was unclear to moderate. Six trials compared dietary advice with standard care, four
compared advice focused on a low-GI diet with advice for a moderate- to high-GI diet, and one compared
dietary advice focused on a high-fibre diet with standard advice. There was a possible reduction in the
development of GDM for women who received dietary advice versus standard care across five trials (1279
women, very low-quality evidence ), though no clear difference for GDM was seen between women who
received low- versus moderate- to high-GI diet advice across four trials (912 women, low-quality evidence ).
Two trials (282 women) reported no clear difference between women who received dietary advice versus
standard care for pre-eclampsia (low-quality evidence ), though fewer women who received dietary advice
developed pregnancy-induced high blood pressure (low-quality evidence ). There was no clear difference
between the groups of women who received low-GI and moderate- to high-GI diet advice, in the number of
babies born large-for-gestational age across three trials (777 babies, very low-quality evidence ). Only one
trial comparing dietary advice with standard care reported on the number of babies who died (either before
birth or shortly afterwards), with no deaths in this trial. There were no clear differences for most of the other
outcomes assessed in the trials comparing dietary advice with standard care. including caesarean section,
perineal trauma, and child skin-fold thickness at six months. However, women who received dietary advice
received gained less weight during their pregnancy across five trials (1336 women) (low-quality evidence ). Similarly,
there were no clear differences for other outcomes assessed in the trials comparing low- and moderate- to
high-GI diet advice, including for caesarean birth and birth weight in pregnancy. The trial comparing dietary
advice focused on a high-fibre diet with standard advice found no clear differences for any outcomes. The
included trials did not report on a large number of outcomes listed in this review, including outcomes relating
to longer-term health for the women and their babies (as children and adults), and the use and cost of health
services. What does this mean? Dietary advice interventions for pregnant women may be able to prevent
GDM. Based on current trials, however, conclusive evidence is not yet available to guide practice. Further
large, well-designed, randomised controlled trials are required to assess the effects of dietary interventions in
pregnancy for preventing GDM and improving other health outcomes for mothers and their babies in the short
and long term. Five trials are ongoing, and four await classification (pending availability of more information)
and will be considered in the next update of this review.

Other Systematic reviews
1. Amin M, Suksomboon N, Poolsup N, Malik O. Comparison of glyburide with metformin in treating


137. Mao H, Li Q, Gao S. Meta-analysis of the relationship between common type 2 diabetes risk gene


194. Rys PM, Ludwig-Slomczynska AH, Cyganek K, Malecki MT. Continuous subcutaneous insulin infusion vs multiple daily injections in pregnant women with type 1 diabetes mellitus: a systematic review and


231. Van Ryswyk E, Middleton P, Hague W, Crowther C. Women's views and knowledge regarding healthcare seeking for gestational diabetes in the postpartum period: A systematic review of


