Exercise for pregnant women for preventing gestational diabetes mellitus (Protocol)

Han S, Crowther CA, Middleton P

This is a reprint of a Cochrane protocol, prepared and maintained by The Cochrane Collaboration and published in The Cochrane Library 2011, Issue 3

http://www.thecochranelibrary.com

WILEY
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Header</td>
<td>1</td>
</tr>
<tr>
<td>Abstract</td>
<td>1</td>
</tr>
<tr>
<td>Background</td>
<td>2</td>
</tr>
<tr>
<td>Objectives</td>
<td>3</td>
</tr>
<tr>
<td>Methods</td>
<td>3</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>8</td>
</tr>
<tr>
<td>References</td>
<td>8</td>
</tr>
<tr>
<td>History</td>
<td>11</td>
</tr>
<tr>
<td>Contributions of Authors</td>
<td>11</td>
</tr>
<tr>
<td>Declarations of Interest</td>
<td>11</td>
</tr>
<tr>
<td>Sources of Support</td>
<td>11</td>
</tr>
</tbody>
</table>
Exercise for pregnant women for preventing gestational diabetes mellitus

Shanshan Han\textsuperscript{1}, Caroline A Crowther\textsuperscript{1}, Philippa Middleton\textsuperscript{1}

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

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

Editorial group: Cochrane Pregnancy and Childbirth Group.

Citation: Han S, Crowther CA, Middleton P. Exercise for pregnant women for preventing gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2011, Issue 3. Art. No.: CD009021. DOI: 10.1002/14651858.CD009021.

Copyright © 2011 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

\textbf{ABSTRACT}

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the effects of physical exercise for pregnant women for preventing glucose intolerance or gestational diabetes.
BACKGROUND

Description of the condition

Introduction and definition of gestational diabetes mellitus

Gestational diabetes mellitus (GDM) is defined as 'any degree of glucose intolerance or hyperglycaemia (high blood glucose level) with onset or first recognition during pregnancy' (Metzger 1998). GDM affects about 1% to 14% of pregnancies around the world and the prevalence is increasing in parallel to increasing rates of maternal obesity and type 2 diabetes mellitus (Bortalico 2007; Debelea 2005; Mulla 2010).

Pathophysiology of gestational diabetes mellitus

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

Health risks for gestational diabetes mellitus

GDM is associated with a range of adverse pregnancy outcomes (Crowther 2005; HAPO Study Cooperative Research Group 2008; Landon 2009; Reece 2009). Women with GDM have the short-term health risks of developing pre-eclampsia and increased need for induction of labour (Crowther 2005; Landon 2009) and caesarean section (Landon 2009). As women with GDM are more likely to have a large-for-gestational age (LGA) or macrosomic (birthweight of 4000 g or more) baby, they are at higher risk of cephalopelvic disproportion, uterine rupture, shoulder dystocia and perineal lacerations (Jastrow 2010). In the longer term, women with GDM have seven to eight times the risk of developing T2DM when compared with those who have had a normoglycaemic pregnancy (Bellamy 2009; Chodick 2010). A comprehensive systematic review found that the cumulative incidence of T2DM in women with GDM ranged from 2.6% to over 70% with a follow-up of six weeks to 28 years postpartum (Kim 2002). Therefore, GDM is usually considered a significant initiating factor in T2DM, and GDM prevention may lead to a decreased rate of type 2 diabetes in successive generations (Mottola 2008).

Babies born to mothers with GDM are more likely to be LGA or macrosomic (HAPO Study Cooperative Research Group 2008; Ju 2008; Reece 2009). LGA or macrosomic infants are at increased risk of injury during birth, such as shoulder dystocia, perinatal asphyxia, bone fractures and nerve palsies (HAPO Study Cooperative Research Group 2008; Henriksen 2008; Langer 2005). Babies of women with GDM are also at higher risk of having other neonatal complications such as respiratory distress syndrome, hypoglycaemia, hyperbilirubinaemia (increased levels of bilirubin in the blood), cardiomyopathy (the deterioration of the function of the heart muscle layer), hypocalcaemia, hypomagnesaemia, polycythaemia, hyperviscosity and admission to neonatal nursery (HAPO Study Cooperative Research Group 2008; Ju 2008; Reece 2009; Soler 1978). In the longer term, children born to mothers with GDM are at increased risk of becoming overweight or obese, developing type 1 and type 2 diabetes and having impaired intellectual achievement (Harder 2009; Mulla 2010; Rizzo 1997; Whincup 2008; Yogev 2009). Infants born LGA are at increased risk of developing the metabolic syndrome (a cluster of risk factors defined by the occurrence of three of the following: obesity, hypertension, hypertriglyceridaemia and low HDL cholesterol concentration) in childhood, adolescence and adulthood (Barker 1994; Guerrero-Romero 2010; Harder 2009). Childhood development of the metabolic syndrome predicts adult type 2 diabetes at 25 to 30 years of age (Morrison 2008). These health problems repeat across generations (Mulla 2010; Petrit 1985).

Risk factors for GDM

There are a range of established risk factors for GDM, some are modifiable and some are non-modifiable (Morisset 2010). The modifiable risk factors include being overweight or obese (body mass index ≥ 25 kg/m² or ≥ 30 kg/m²); physical inactivity or sedentary lifestyle; low fibre and high glycaemic load diet; history of having a macrosomic (birthweight ≥ 4000 g) infant; and history of GDM (Chasan-Taber 2008; Mottola 2008; Petry 2010; Zhang 2006). Non-modifiable risk factors include advanced maternal age, nonwhite race/ethnicity, family history of diabetes mellitus, maternal high or low birthweight, high parity, polycystic ovarian syndrome (Cypryk 2008; Petry 2010; Solomon 1997).

Management of GDM

The primary aims of treatment for GDM are to optimise glycaemic control and improve pregnancy outcomes (Aiwan 2009). Management includes any or all of: diet and lifestyle advice, use of oral glucose-lowering agents (e.g. metformin, glyburide), administration of insulin, fetal surveillance (e.g. doppler umbilical blood flow measurement, cardiotocograph and ultrasonography) and maternal glucose monitoring (Hoffman 1998; Metzger 2007; NICE 2008).

Providing dietary and lifestyle advice is usually recommended as the primary therapeutic strategy for women with GDM to achieve acceptable glycaemic control (ACOG 2001; Hoffman 2002).
To continue or start moderate intensity exercise is encouraged for women without medical or obstetrical contraindications as part of treatment for GDM (ADA 2003; Hoffman 1998; NICE 2008). If these interventions alone are not enough to achieve good maternal glycaemia control, insulin therapy may be indicated (ACOG 2001; Hoffman 1998; NICE 2008). Oral hypoglycaemics such as glyburide and metformin may be used as alternatives to insulin therapy (Silva 2010; Simmons 2004). As a part of management for GDM, maternal glucose monitoring and ultrasonography are advised to monitor treatment and guide care for birth (ACOG 2001; Hoffman 1998; NICE 2008).

**Description of the intervention**

**Physical activity and pregnancy**

Until several decades ago, physical activity had been discouraged in pregnancy due to theoretical concerns of exercise-induced injury and adverse fetal and maternal outcomes (Dempsey 2005; Schlüssel 2008). Since the early 21st century, the benefits of exercise during pregnancy have been realised and pregnant women have been encouraged to have regular physical activity in the absence of medical or obstetric complications (Dempsey 2005; Schlüssel 2008). Light to moderate physical activity during a normal pregnancy provides various benefits for mother and fetus (Melzer 2010). For mothers, it helps reduce and prevent lower back pain, decreases liquid retention, reduces cardiovascular stress, increases oxygenation capacity, decreases blood pressure, and helps control gestational weight gain (Melzer 2010; Schlüssel 2008). Fetal benefits include decreased fat mass, reduced risk of being a large for gestational age fetus, improved stress tolerance, and advanced neurobehavioural maturation (Melzer 2010; Snapp 2008). Recent observational studies have found physical activity during normal pregnancy decreased insulin resistance and therefore might help to decrease the risk of GDM (Redden 2010; Reece 2009). Some evidence has suggested that the risk of GDM was decreased by 20% to 55% among women with physical exercise of various duration and intensity before or during pregnancy (Dempsey 2004a; Dempsey 2004b; Oken 2006; Zhang 2006).

**How the intervention might work**

Acute exercise and recurrent weight-bearing exercise were found to decrease circulating glucose and insulin concentrations during and for a period of time after exercise sessions (Clapp 1991; Clapp 1998). The effect was greatest with low-intensity prolonged exercise that utilises a large muscle mass in late pregnancy shortly (less than two hours) after mixed caloric intake (Clapp 2006). Investigators have shown that physical exercise was effective in preventing and managing type 2 diabetes by reducing insulin resistance in non-pregnant women and men (Clapp 2006; Knowler 2002; Oken 2006; Redden 2010). Regular exercise during pregnancy is associated with decreased circulating TNF-α levels in a dose- and time-dependent manner (Clapp 2000). These research findings suggest that physical exercise during normal pregnancy may be effective in preventing GDM.

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

GDM affects a significant proportion of pregnant women each year and the prevalence is increasing worldwide (Bottalico 2007; Debelea 2005; Mulla 2010). GDM is associated with a range of negative pregnancy outcomes and these adverse health outcomes can repeat across generations (HAPO Study Cooperative Research Group 2008; Mulla 2010). Therefore, identifying ways that might help prevent GDM is of urgent public health importance. Although the risk factors and health outcomes of GDM have been well recognised, there is little known about the ways to prevent GDM in high-risk populations (Mottola 2008; Petry 2010; Pivarnik 2006). Physical exercise, as one of the modifiable risk factors for GDM, has attracted great attention in recent years (Melzer 2010). There has been a suggestion that physical exercise before and during pregnancy may be effective in preventing GDM; however, little robust evidence from randomised controlled trials (RCTs) is available (Petry 2010). This review will help to provide reliable evidence for pregnant women on the effects of physical exercise on GDM prevention. Another two Cochrane reviews have addressed the effects of exercise for diabetic pregnant women (Ceyzens 2006) and the role of aerobic exercise for healthy pregnant women (Kramer 2006).

**OBJECTIVES**

To assess the effects of physical exercise for pregnant women for preventing glucose intolerance or gestational diabetes.

**METHODS**

**Criteria for considering studies for this review**

**Types of studies**

All published RCTs assessing the effects of physical exercise in preventing pregnancy glucose intolerance or GDM. We will include cluster trials. We will also include published abstracts for RCTs and cluster-RCTs if relevant outcome data are available. We will exclude quasi-RCTs and crossover trials.
We will include trials assessing the effects of lifestyle interventions (e.g., include both nutrition and physical exercise interventions) in preventing pregnancy glucose intolerance or GDM if we are able to extract data for the effects of physical exercise separately.

**Types of participants**
Pregnant women regardless of age, gestation, parity or plurality. We will exclude women with pre-existing type 1 and type 2 diabetes.

**Types of interventions**
Interventions will include any types of exercise and lifestyle management (i.e., exercise advice, providing exercise sessions) for pregnant women for preventing GDM before screening tests. One type of intervention can be compared to standard antenatal care, i.e., any type of exercise advice (standard advice or individualised advice) compared with standard antenatal care; providing exercise sessions (group exercise or individual exercise session) compared with standard care. Multiple forms of interventions can be compared with standard care, i.e., providing exercise advice and exercise sessions compared with standard care. Two forms of interventions can be compared with each other, i.e., providing exercise advice compared with providing exercise session. Two or more types of the same form of management can be compared against each other, i.e., standard exercise advice compared with individualised exercise advice; group exercise session compared with individual exercise session; different intensities of exercise sessions compared with each other; exercise interventions only compared with exercise interventions plus other forms of intervention (e.g., providing dietary advice).

**Types of outcome measures**

**Primary outcomes**

**Maternal outcomes**
1. Incidence of gestational diabetes mellitus (diagnostic criteria as defined in individual trials)
2. Mode of birth (normal vaginal birth, operative vaginal birth, caesarean section)

**Fetal/neonatal outcomes**
1. Large-for-gestational age
2. Perinatal mortality (fetal and neonatal mortality)

**Secondary outcomes**

**Maternal outcomes**

**Perinatal**
1. Incidence of pregnancy hyperglycaemia not meeting GDM diagnostic criteria (diagnostic criteria as defined in individual trials)
2. Induction of labour
3. Perineal trauma
4. Pre-eclampsia
5. Weight gain during pregnancy
6. Gestational age at screening for gestational diabetes mellitus
7. Postpartum haemorrhage
8. Postpartum infection
9. Placental abruption
10. Adherence to exercise intervention
11. Women’s sense of well-being and quality of life (defined by author(s))
12. Women’s view of intervention

**Long term**
1. Postnatal weight retention
2. BMI
3. Gestational diabetes in subsequent pregnancy
4. Development of type 2 diabetes mellitus
5. Development of type1 diabetes mellitus
6. Impaired glucose tolerance (defined by author(s))
7. Insulin sensitivity (defined by author(s))

**Fetal/neonatal outcomes**
1. Macrosomia (birthweight greater than 4000 g)
2. Birthweight
3. Small-for-gestational age
4. Neonatal hypoglycaemia requiring treatment (variously defined by authors of individual trials)
5. Gestational age at birth
6. Preterm birth (less than 37 weeks’ gestation)
7. Shoulder dystocia
8. Bone fracture
9. Nerve palsy
10. Respiratory distress syndrome
11. Hyperbilirubinaemia requiring treatment (variously defined by authors of individual trials)
12. Apgar scores (less than seven at five minutes)
13. Ponderal index
14. Skinfold thickness measurements
Childhood outcomes
1. Weight
2. Height
3. BMI
4. Fat mass/fat-free mass
5. Skinfold thickness measurements
6. Blood pressure
7. Impaired glucose tolerance (as defined by author(s))
8. Development of type 1 diabetes
9. Development of type 2 diabetes
10. Insulin sensitivity (as defined by author(s))
11. Dyslipidaemia or metabolic syndrome
12. Neurodisability
13. Educational achievement

Adulthood outcomes
1. Weight
2. Height
3. BMI
4. Fat mass/fat-free mass
5. Skinfold thickness measurements
6. Blood pressure
7. Impaired glucose tolerance (defined by author(s));
8. Development of type 1 diabetes;
9. Development of type 2 diabetes;
10. Insulin sensitivity (defined by author(s));
11. Dyslipidaemia or metabolic syndrome
12. Educational achievement

Health services cost
1. Number of hospital visits or health professional visits (e.g. physiotherapist) or antenatal visits for mother
2. Medical physician visits
3. Costs to families in relation to the management provided
4. Length of postnatal stay (mother)
5. Admission to neonatal ward
6. Length of postnatal stay (baby)
7. Cost of maternal care
8. Cost of offspring care

Search methods for identification of studies

Electronic searches
We will contact the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register.

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

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

We will not apply any language restrictions.

Data collection and analysis

Selection of studies
Two review authors will independently assess for inclusion all the potential studies we identify as a result of the search strategy. We will resolve any disagreement through discussion or, if required, we will consult a third person.

Data extraction and management
We will design a form to extract data. For eligible studies, at least two review authors will extract the data using the agreed form. We will resolve discrepancies through discussion or, if required, we will consult a third person. We will enter data into Review Manager software (RevMan 2008) and check for accuracy.

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

Assessment of risk of bias in included studies
Two review authors will independently assess risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2009). We will resolve any disagreement by discussion or by involving a third assessor.

(1) Sequence generation (checking for possible selection bias)
We will describe for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.
We will assess the method as:
• adequate (any truly random process, e.g. random number table; computer random number generator);
• inadequate (any non-random process, e.g. odd or even date of birth; hospital or clinic record number); or
• unclear.

(2) Allocation concealment (checking for possible selection bias)
We will describe for each included study the method used to conceal the allocation sequence and determine whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment. We will assess the methods as:
• adequate (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
• inadequate (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
• unclear.

(3) Blinding (checking for possible performance bias)
We will describe for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We will consider that studies are at low risk of bias if they were blinded, or if we judge that the lack of blinding could not have affected the results. We will assess blinding separately for different outcomes or classes of outcomes. We will assess the methods as:
• adequate, inadequate or unclear for participants;
• adequate, inadequate or unclear for personnel;
• adequate, inadequate or unclear for outcome assessors.

(4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)
We will describe for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We will state whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information is reported, or can be supplied by the trial authors, we will re-include missing data in the analyses which we undertake. We will assess methods as:
• adequate (when there is no missing data, or missing data is balanced across groups and judged unlikely to influence the outcome, or missing data have been imputed using appropriate methods);
• inadequate (when data is missing, and this is judged to potentially alter the findings of the study);
• unclear.

(5) Selective reporting bias
We will describe for each included study how we investigated the possibility of selective outcome reporting bias and what we found. We will assess the methods as:
• adequate (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
• inadequate (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
• unclear.

(6) Other sources of bias
We will describe for each included study any important concerns we have about other possible sources of bias. We will assess whether each study was free of other problems that could put it at risk of bias:
• yes;
• no;
• unclear.

(7) Overall risk of bias
We will make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the Handbook (Higgins 2009). With reference to (1) to (6) above, we will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We will explore the impact of the level of bias through undertaking sensitivity analyses - see Sensitivity analysis.

Measures of treatment effect

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

Continuous data
For continuous data, we will use the mean difference if outcomes are measured in the same way between trials. We will use the standardised mean difference to combine trials that measure the same outcome, but use different methods.
Unit of analysis issues

Cluster-randomised trials

We will include cluster-randomised trials in the analyses along with individually randomised trials. We will adjust their sample sizes using the methods described in the Handbook using an estimate of the intraclass correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population (Higgins 2009). If we use ICs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely.

We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Dealing with missing data

For included studies, we will note levels of attrition. We will explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis.

For all outcomes, we will carry out analyses, as far as possible, on an intention-to-treat basis, i.e. we will attempt to include all participants randomised to each group in the analyses, and all participants will be analysed in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial will be the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

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

Assessment of reporting biases

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

Data synthesis

We will carry out statistical analysis using the Review Manager software (RevMan 2008). We will use fixed-effect meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect: i.e. where trials are examining the same intervention, and the trials’ populations and methods are judged sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if we detect substantial statistical heterogeneity, we will use random-effects meta-analysis to produce an overall summary if an average treatment effect across trials is considered clinically meaningful. We will treat the random-effects summary as the average range of possible treatment effects and we will discuss the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful we will not combine trials.

If we use random-effects analyses, we will present the results as the average treatment effect with its 95% confidence interval, and the estimates of T² and I².

Subgroup analysis and investigation of heterogeneity

If we identify substantial heterogeneity, we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, use random-effects analysis to produce it.

Maternal characteristics, and characteristics of exercise interventions are likely to affect health outcomes. We plan to carry out the following subgroup analyses.

1. Maternal characteristics
   - Maternal age
     - We will compare 35 years of age or more with less than 35 years of age
   - Maternal BMI (at or before trial entry)
     - We will compare BMI ranges of 18.5 to 24.9 kg/m² with those of less than 18.5 kg/m²;
     - BMI ranges of 18.5 to 24.9 kg/m² with those of 25 to 29.9 kg/m²;
     - BMI ranges of 18.5 to 24.9 kg/m² with those of 30 kg/m² to 39.9 kg/m²;
     - BMI ranges of 18.5 to 24.9 kg/m² with those of 40 kg/m² or more.
   - Ethnicity
     - We will compare high risk-ethnic group with low-risk ethnic group.
Parity
- We will compare parity of 0 with 1-2;
- parity of 0 with 3 or more.

2. Nature of exercise interventions
- We will compare exercise intervention only with exercise intervention plus other forms of intervention (e.g. dietary advice);
  - frequency of the intervention:
    - we will compare frequencies of one to four times/week with five or more times/week;
  - duration of the intervention:
    - we will compare less than 20 minutes per session with 20 minutes or more per session;
  - intensity of the exercise sessions:
    - we will compare light intensity exercise with moderate intensity exercise;
    - we will compare light intensity exercise with high intensity exercise.

*intensity of exercise is defined by individual trials.

3. Ways of delivering intervention
- We will compare exercise advice only with providing exercise sessions;
- face-to-face intervention with non-face-to-face intervention (e.g. phone counselling, information package etc.);
- group intervention with individual intervention.

We will use primary outcomes in subgroup analyses. For fixed-effect inverse variance meta-analyses we will assess differences between subgroups by interaction tests. For random-effects and fixed-effect meta-analyses using methods other than inverse variance, we will assess differences between subgroups by inspection of the subgroups’ confidence intervals; non-overlapping confidence intervals indicate a statistically significant difference in treatment effect between the subgroups.

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

ACKNOWLEDGEMENTS
As part of the pre-publication editorial process, this protocol has been commented on by two peers (an editor and referee who is external to the editorial team), a member of the Pregnancy and Childbirth Group’s international panel of consumers and the Group’s Statistical Adviser.

REFERENCES

Additional references

ACOG 2001

ADA 2003

Alwan 2009

Barker 1994

**Clapp 1991**

**Clapp 1998**

**Clapp 2000**

**Clapp 2006**

**Crowther 2005**

**Cypryk 2008**

**Debelea 2005**

**Dempsey 2004a**

**Dempsey 2004b**

**Dempsey 2005**

**Devlieger 2008**
Devlieger R, Castreels K, Van Assele FA. Reduced adaptation of the pancreatic B cells during pregnancy is the major causal factor for gestational diabetes: current knowledge and metabolic effects on the offspring. *Acta Obstetricia et Gynecologica Scandinavica* 2008;87(12):1266–70.

**Egger 1997**

**Guerrero-Romero 2010**

**HAPO Study Cooperative Research Group 2008**

**Harbord 2006**

**Harder 2009**

**Henriksen 2008**

**Higgins 2009**

**Hoffman 1998**

**Jastrow 2010**

**Ju 2008**
Exercise for pregnant women for preventing gestational diabetes mellitus (Protocol)

Copyright © 2011 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Kim 2002

Knowler 2002

Kramer 2006

Landon 2009

Langer 2005

Melzer 2010

Metzger 1998

Metzger 2007

Morisset 2010

Morrison 2008

Mottola 2010

Mulla 2010

NICE 2008

Oken 2006

Petit 1985

Petry 2010

Pivarnik 2006

Redden 2010

Recce 2009

RevMan 2008

Rizzo 1997

Schlüssel 2008
Silva 2010

Simmons 2004

Snapp 2008

Soler 1978

Solomon 1997

Whincup 2008

Yogev 2009

Zhang 2006

* Indicates the major publication for the study

HISTORY

CONTRIBUTIONS OF AUTHORS
Shanshan Han wrote the first draft of the protocol, with Caroline Crowther and Philippa Middleton making comments and contributing to subsequent drafts.

DECLARATIONS OF INTEREST
None known.

SOURCES OF SUPPORT

Internal sources
- ARCH, Robinson Institute, The University of Adelaide, Australia.
External sources

- Australian Department of Health and Ageing, Australia.