Version

This is the publisher’s version. This version is defined in the NISO recommended practice RP-8-2008 http://www.niso.org/publications/rp/

Suggested Reference


Copyright

Items in ResearchSpace are protected by copyright, with all rights reserved, unless otherwise indicated. Previously published items are made available in accordance with the copyright policy of the publisher.

This review is published as a Cochrane Review in the Cochrane Database of Systematic Reviews 2016, 10. Cochrane Reviews are regularly updated as new evidence emerges and in response to comments and criticisms, and the Cochrane Database of Systematic Reviews should be consulted for the most recent version of the Review.

For more information, see General copyright, Publisher copyright, SHERPA/RoMEO.
Interventions for preventing gestational diabetes mellitus: an overview of Cochrane Reviews (Protocol)


www.cochranelibrary.com
# Table of Contents

- Header ................................................................. 1
- Abstract ........................................................................ 1
- Background ............................................................... 1
- Objectives ...................................................................... 3
- Methods ......................................................................... 4
- Acknowledgements ...................................................... 6
- References ...................................................................... 7
- Appendices ..................................................................... 12
- Contributions of Authors ............................................... 14
- Declarations of Interest .................................................. 15
- Sources of Support ........................................................ 15
Overview of Reviews Protocol

Interventions for preventing gestational diabetes mellitus: an overview of Cochrane Reviews

Robyn L Lawrence¹, Julie Brown¹, Philippa Middleton², Emily Shepherd³, Stephen Brown⁴, Caroline A Crowther¹,³

¹Liggins Institute, The University of Auckland, Auckland, New Zealand. ²Healthy Mothers, Babies and Children, South Australian Health and Medical Research Institute, Adelaide, Australia. ³ARCH: Australian Research Centre for Health of Women and Babies, Robinson Research Institute, Discipline of Obstetrics and Gynaecology, The University of Adelaide, Adelaide, Australia. ⁴School of Interprofessional Health Studies, Auckland University of Technology, Auckland, New Zealand

Contact address: Julie Brown, Liggins Institute, The University of Auckland, Private Bag 92019, Victoria Street West, Auckland, 1142, New Zealand. j.brown@auckland.ac.nz.

Editorial group: Cochrane Pregnancy and Childbirth Group.


Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Abstract

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

To summarise the evidence from Cochrane systematic Reviews regarding the effects of interventions for preventing gestational diabetes mellitus.

Background

Description of the condition

Rates of gestational diabetes mellitus (GDM), defined as hyperglycaemia with blood glucose values above normal, but below those diagnostic of diabetes which occurs during pregnancy and usually returning to normal after birth (WHO 2013), are rising worldwide (Ferrara 2007). Women with GDM have a greater degree of insulin resistance compared with women without GDM, which leads to maternal hyperglycaemia and transport of glucose across the placenta to the developing fetus (Setji 2005). GDM is thought to result from an inadequate compensatory response to this insulin-resistant state caused by hormonal changes in pregnancy (Buchanan 1990; Setji 2005). The multifaceted aetiology of GDM is demonstrated in its many risk factors, which include advanced maternal age, maternal obesity, certain ethnicities, family history of diabetes, and previous history of GDM, macrosomia or neonatal death (Berkowitz 1992; Chu 2007; Khan 2013; Solomon 1997; Theriault 2014; Xiong 2001). Whilst a number of risk factors have been identified, exactly how each contributes to the development of GDM is uncertain. Nevertheless, some of these risk factors are modifiable and can be targeted in preventive interventions.

Health risks for women with GDM include pre-eclampsia and induction of labour (Crowther 2005), and more than half will develop type 2 diabetes within 10 years after giving birth (Kim 2002). There are well-documented risks for infants born to mothers with GDM, including being large-for-gestational age, macrosomia, respiratory distress syndrome, jaundice, hypoglycaemia, and birth injuries such as nerve palsy, bone fracture and shoulder dysto-
Increased muscle activity (Adams 1998; Crowther 2005; Gonzalez-Quintero 2007; He 2015; Landon 2009; Langer 2005). In addition there is increasing recognition of intraterumine programming effects and adverse long-term health consequences into childhood and adulthood that include obesity, diabetes, and the metabolic syndrome (Boney 2005; Cho 2000).

**Description of the interventions**

Given the multifaceted aetiology of GDM, interventions aimed at preventing GDM may target a variety of risk factors. Multiple approaches, including diet, physical activity, dietary supplements and pharmaceutical interventions, have been proposed for GDM prevention. Interventions are often multifaceted, combining one or more approaches.

Food-based interventions have focused primarily on minimising the impact of diet on glycaemic response through low glycaemic index or high fibre diets (Frazier 1983; Frazier 1988; Markovic 2015). The role of a number of dietary supplements in preventing GDM, such as probiotics, myo-inositol, vitamin D and fish oils, have also been investigated (D’Anna 2013; Lindsay 2014; Soheilykah 2013; Zhou 2012). Interventions aimed at increasing physical activity have ranged from the provision of advice to supervised group or individualised exercise sessions including aerobic activities, stationary cycling or yoga (Barakat 2012; Ong 2009; Rakhshani 2012; Stafne 2012). Physical activity interventions have been administered either alone (Barakat 2012; Ong 2009; Stafne 2012) or in combination with a dietary intervention (Dodd 2014; Luoto 2011).

There are a number of oral anti-diabetic pharmaceutical therapies, including sulfonylureas, biguanides, thiazolidinediones, alpha-glucosidase inhibitors, meglitinides and peptide analogues, although the safety of many of these for use in pregnancy is unclear (Holt 2014; Slocum 2002). Metformin or glibenclamide are the only oral hypoglycaemics recommended for use in pregnancy (ACOG 2013; NICE 2015), although these are not currently licensed for use in pregnancy (Skupien 2014). Interventions identified as having a potential role in the prevention of GDM have also targeted women at preconception or interconception time points, particularly in women at high risk of GDM such as those who are overweight or obese (Yeung 2010) or have a history of GDM (Khan 2013).

**How the intervention might work**

**Dietary interventions**

A number of components of the diet may influence GDM risk through direct and indirect effects on glycaemic response, and these may have an additive effect (Ley 2011; Rogozinska 2015; Zhang 2006). High intake of simple sugars has been associated with reduced insulin sensitivity and insulin secretion (Davis 2005; Reiser 1979), while intake of whole grain foods, cereal fibre and low glycaemic index foods have been associated with lower insulin resistance. Chronic increased insulin demand through a high intake of simple sugars may lead to pancreatic exhaustion, resulting in glucose intolerance (Ludwig 2002). On the other hand, fibre intake slows digestion (Burton-Freeman 2000; Jenkins 2000; Vahouny 1988) and glucose absorption, resulting in an attenuated blood glucose and insulin response (Jenkins 2000; Liese 2005; Mcintosh 2001). Increased dietary fibre may reduce appetite, lowering total energy intake, thereby reducing adiposity and its associated insulin resistance (Burton-Freeman 2000). Protein and dietary fats may play a role in GDM development through their effects on satiety (Tannous dit El Khoury 2006), adiposity (Kantarzis 2009; Kohrt 1993; Pan 1993) and inflammation (Cai 2012; Lin 2012).

Calorie restriction may reduce the risk of GDM through consequent weight loss and reduced fat mass, leading to improvements in insulin sensitivity and glycaemic status (Knopp 1991; Larson-Meyer 2006). However, excessive calorie restriction can lead to ketonaemia and ketonuria through starvation ketosis (Magee 1990; Metzger 2007). Reports of detrimental effects of maternal ketones on foetal development has raised concerns about the safety of severe calorie restriction and weight loss during pregnancy (Churchill 1969; Ornoy 1998; Rizzo 1991). A number of agencies recommend avoiding hypocaloric diets during pregnancy (Health Service Executive Ireland 2010; NICE 2010; Thompson 2013), but some suggest calorie restriction may be appropriate in overweight and obese pregnant women (Academy of Nutrition and Dietetics 2008; Knopp 1991).

**Physical activity interventions**

Regular physical activity, both before and during pregnancy, has been associated with a reduced risk of GDM (Dempsey 2004; Zhang 2014). Physical activity affects energy expenditure and therefore directly affects glucose utilisation. Physical activity enhances glucose uptake through translocation of the glucose transporter type 4 (GLUT-4) on skeletal muscle (Kennedy 1999). Insulin sensitivity is increased with physical activity, with effects continuing after exercise is ceased (Persghin 1996). Increased muscle mass as a result of physical activity is likely to further improve glucose tolerance and increase insulin sensitivity (Yki-Jarvinen 1983).
Probiotics

Probiotics are live micro-organisms that, when administered in adequate amounts, may confer a health benefit to the host (FAO/WHO 2001; Hill 2014). Probiotics may improve insulin resistance by changing the microbiota of the gut (FAO/WHO 2001; Hill 2014; Kondo 2010) through their effects on reducing inflammatory signalling (Ma 2008), and up-regulating genes related to fat metabolism and insulin sensitivity and decreasing adiposity (Kondo 2010).

Myo-inositol

Myo-inositol is a polyol (Croze 2013) that occurs naturally in the diet, is present in certain fruit, vegetables, beans, nuts, seeds and grains, (Clements 1980) and is thought to mimic the action of insulin (Croze 2013; Saltiel 1990). Myo-inositol acts as a mediator in the insulin-signalling cascade (Baillargeon 2010), and has been shown to improve insulin sensitivity (Corrado 2011) through the enhancement of GLUT-4 translocation in skeletal muscle (Dang 2010).

Vitamin D

Vitamin D has been positively associated with insulin sensitivity and pancreatic β-cell function (Chiu 2004). It is thought that vitamin D may affect insulin secretion by binding to vitamin D receptors in the pancreas and regulating the balance between the extracellular and intracellular calcium pools (Sooy 1999). In animal models, vitamin D deficiency reduces pancreatic insulin secretion (Bourlon 1999; Norman 1980), while supplementation with vitamin D can influence the expression of insulin-sensitive genes (Alkharfy 2013), reduce inflammatory markers and improve glucose uptake (Marcotorchino 2012).

Fish oil

Differences in circulating concentrations of long-chain polyunsaturated fatty acids are seen in women with GDM compared with women without GDM (Wijendran 1999). It has been hypothesised that omega-3 long-chain polyunsaturated fatty acids consumed in the diet, primarily in the form of oily fish or fish oil supplements (Kris-Etherton 2000; Kris-Etherton 2009), are incorporated into peripheral and pancreatic cell membranes. This is thought to enhance insulin secretion, insulin receptor binding and insulin sensitivity, thereby enhancing glucose transport across peripheral cell membranes and improving glucose homeostasis (Lardinois 1987). Omega-3 fatty acids may further modulate diabetes risk through their anti-inflammatory properties (Calder 2006).

Pharmaceutical interventions

Metformin improves insulin sensitivity and hyperglycaemia (Jackson 1987) by reducing gluconeogenesis in the liver (Stumvoll 1995; Wollen 1988) and enhancing peripheral glucose uptake and utilisation by altering metabolic pathways (Viollet 2012). Metformin may therefore protect against GDM by reducing insulin resistance and preserving pancreatic β-cell reserves during pregnancy, when both insulin resistance and insulin secretion are increased (Kazi 2015).

Preconception or interconception interventions

Preconception and interconception are key time points for the identification of risk factors for complications during pregnancy, including GDM, and are opportune times to provide advice on strategies to improve health and pregnancy outcomes (Hanson 2015; Jack 1990). Targeting modifiable risk factors such as weight gain, overweight or obesity may reduce the risk of GDM in subsequent pregnancies (Pole 1999).

Why it is important to do this overview

GDM affects an increasing number of pregnant women each year, posing significant health risks to both mother and infant. A number of risk factors for GDM, such as physical inactivity and being overweight or obese prior to pregnancy, are potentially modifiable and while different strategies have shown promise in the prevention of GDM, it is currently unclear which strategies are effective. Primary prevention of GDM rather than treatment would lead to economic (Danyliv 2014) and health benefits. This overview will provide an important resource for all healthcare professionals caring for pregnant women, guideline developers, policy makers, researchers, women who are at risk of developing GDM and their families. Use of the overview to identify and then target effective preventive interventions may contribute to reducing the incidence of GDM and the associated short- and long-term health risks for the mother and her child. Further, this overview may identify areas requiring further research.

OBJECTIVES

To summarise the evidence from Cochrane systematic Reviews regarding the effects of interventions for preventing gestational diabetes mellitus.
METHODS

Criteria for considering reviews for inclusion

In this overview of systematic reviews, we will include only published Cochrane systematic Reviews, assessing interventions for prevention of gestational diabetes mellitus (GDM), reporting GDM as a primary or secondary review outcome. We will identify Cochrane protocols and titles for future inclusion, and classify them as ‘ongoing reviews’ (in an appendix). If a review identified for inclusion is more than two years out of date, we will contact the review authors to ascertain when the review will be updated. If such a review is out of date and is not going to be updated in time to be included in the overview, we will include the last published version and acknowledge this as a limitation.

Participants

We will include reviews that cover women planning a pregnancy or pregnant women. We will exclude reviews covering women with pre-existing type 1 or type 2 diabetes.

Interventions

We will include lifestyle, dietary supplement, pharmacological and other interventions used to prevent GDM and implemented prior to GDM screening, including:

1. dietary interventions;
2. physical activity interventions;
3. combined dietary and physical activity interventions;
4. dietary supplement interventions (e.g. probiotics, myo-inositol, vitamin D and omega-3 fatty acids);
5. pharmaceutical interventions (e.g. oral anti-diabetic pharmaceutical therapies);
6. other interventions for prevention not detailed above.

We will include Cochrane systematic Reviews evaluating interventions administered at preconception, interconception and during pregnancy. We will include reviews evaluating interventions compared with a control, as well as those evaluating one intervention compared with another intervention.

Outcomes

Primary outcomes

Maternal outcomes

• Diagnosis of GDM (as defined by systematic review authors)

• Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension and eclampsia)
• Caesarean section

Child (as a fetus, neonate, child, adult) outcomes

• Large-for-gestational age
• Perinatal mortality (stillbirth and neonatal mortality)
• Composite outcome of serious neonatal outcomes

Secondary outcomes

Maternal outcomes

• Perineal trauma
• Gestational weight gain
• Postnatal depression
• Development of subsequent diabetes

Child (as a fetus, neonate, child, adult) outcomes

• Neonatal hypoglycaemia
• Offspring adiposity
• Offspring diabetes
• Neurosensory disability

Health service use outcomes

• Number of antenatal visits or admissions
• Length of postnatal stay (mother)
• Length of postnatal stay (baby)
• Costs to families associated with the management provided
• Costs associated with the intervention
• Cost of maternal care
• Cost of offspring care (including neonatal intensive care unit admission)

Search methods for identification of reviews

We will search the Cochrane Database of Systematic Reviews for any systematic reviews or protocols that examine interventions for the preventing GDM. Key words that we will use for the search are ‘gestational diabetes’ OR ‘GDM’ OR ‘diabetes AND pregnancy’. We will use the search terms to search ‘all text’, and not limited to ‘title, abstract, or keywords’. We will not apply any language or date restrictions.
Data collection and analysis

We will base the methodology for data collection and synthesis on Chapter 22, ‘Overviews of Reviews’ in the Cochrane Handbook of Systematic Reviews of Interventions (Becker 2011).

Selection of reviews

Two overview authors will independently assess for potential inclusion all Cochrane systematic Reviews we identify that evaluate the effects of interventions for GDM prevention. We will resolve any disagreement through discussion or, if required, through consultation with a third overview author.

Data extraction and management

Two of the overview authors will independently extract data, using an electronic form which we will design and pilot. We will resolve disagreements by consensus or by recourse to a third overview author. If any information from the reviews is missing, we will contact the systematic review authors for further details. We will extract and tabulate information for the following:

Review characteristics

- Review title and authors.
- Search date: date of search conducted by review (we will consider less than two years ago to be current).
- The number of trials in the review, number of women and their infants.
- The population demographics: we will produce a summary of the participant characteristics in the included reviews.
- Quality of the included trials (as reported by the review authors; see ‘Quality of included studies within reviews’ below, under Assessment of methodological quality of included reviews).
- Interventions and comparisons relevant to this overview.
- All prespecified outcomes relevant to this overview as listed below.
- Any other characteristics required to assess and report on review quality (see ‘Quality of included reviews’ under Assessment of methodological quality of included reviews).

Outcomes

Maternal outcomes:
- Diagnosis of GDM
- Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension and eclampsia)
- Gestational weight gain
- Caesarean section
- Perinatal trauma
- Postnatal depression
- Development of subsequent diabetes

Child (as a fetus, neonate, child, adult) outcomes:
- Large-for-gestational age
- Perinatal mortality (stillbirth and neonatal mortality)
- Composite outcome of serious neonatal outcomes
- Neonatal hypoglycaemia
- Offspring adiposity
- Offspring diabetes
- Neurosensory disability

Health service use outcomes:
- Number of antenatal visits or admissions
- Length of postnatal stay (mother)
- Length of postnatal stay (baby)
- Cost to families associated with the management provided
- Costs associated with the intervention
- Cost of maternal care
- Cost of offspring care (including neonatal intensive care unit admission)

Statistical summaries

- Summary intervention effects by intervention, including the pooled effects (e.g. risk ratios, odds ratios, mean differences, standardised mean differences, or numbers needed to treat), 95% confidence intervals, and numbers of studies and participants contributing data to each pooled effect for the overview’s maternal and child outcomes.
- Information required to assess and report on the quality of the evidence for the intervention effects extracted above (see ‘Quality of evidence in included reviews’ under Assessment of methodological quality of included reviews).
- Where reviews were not able to perform meta-analyses and therefore did not report statistical summaries, we plan to extract from those reviews the narrative text relating to the results for our overview outcomes.

To describe the extent of the evidence available from the systematic reviews of interventions included in the overview, we will include a table (as an appendix) that uses the outcomes agreed on by consensus by the authors of Cochrane systematic Reviews for prevention and treatment of GDM (Appendix 1), and shows for each systematic review included in the overview whether or not there were data for these outcomes included in the systematic review, and will document any additional outcomes that the systematic review reported. We will not extract data for all these outcomes but only data for the GRADE outcomes prespecified for this overview.

Assessment of methodological quality of included reviews

Quality of included reviews
We will assess the methodological quality of each systematic review using the ROBIS (Risk of Bias in Systematic reviews) tool (Whiting 2015). The ROBIS tool consists of three phases; the first assesses the relevance of the systematic review to the research question, the second identifies concerns with the review process, and the third judges the risk of bias across four domains.

- Study eligibility criteria
- Identification and selection of studies
- Data collection and study appraisal
- Synthesis and findings

Signalling questions are used to assess specific concerns about potential biases within the review, and the ratings from these questions are used to judge overall risk of bias. The signalling questions are answered as ‘yes’, ‘probably yes’, ‘probably no’, ‘no’ or ‘no information’. The subsequent level of concern about bias associated with each domain is then judged as ‘low’, ‘high’, or ‘unclear’. If the answers to all signalling questions for a domain are ‘yes’ or ‘probably yes’, the level of concern can be judged as low. If any signalling question is answered ‘no’ or ‘probably no’, the potential for concern about bias exists.

Quality of evidence in the included reviews

We will assess the quality of the evidence from each review using the GRADE system for the outcomes listed above. Where available, we will use the GRADE 'Summary of findings' tables from the included Cochrane systematic Reviews. Where such a table is not available, we will produce one using GRADE Profiler software (GRADEpro). The GRADE system assesses the following features for the evidence found for selected outcomes.

- Risk of bias: internal validity of the evidence
- Inconsistency: heterogeneity or variability in the estimates of effect across studies
- Indirectness: degree of differences between population, intervention and outcome of interest
- Imprecision (random error): extent to which confidence in the effect estimate is adequate to support a particular decision
- Risk of publication bias: degree of selective publication of studies

The GRADE system rates the quality of the evidence as:

- high (further research is very unlikely to change confidence in the estimate of the effect);
- moderate (further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate);
- low (further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate);
- very low (any estimate of effect is very uncertain).

We will summarise the evidence in an 'Overview of reviews' table which we will populate with the summary risk estimate and 95% confidence interval, number of participants, and the quality of evidence for each outcome, grouped by intervention topic, timing of intervention (preconception, interconception and during pregnancy) and whether GDM was a primary or secondary outcome.

Quality of included studies within reviews

We will not reassess the quality of included studies within reviews, but instead will report study quality according to the review authors' assessment. In the case that individual studies are included in two or more Cochrane Reviews, we will report this, and any variation regarding review authors' assessments of study quality. We will collect this information during the data extraction process. We will resolve disagreements by discussion.

Data synthesis

We will undertake a narrative description of the included Cochrane systematic Reviews, and their summary statistics. We will not examine indirect comparisons and will not conduct network meta-analyses. We will summarise the main results of the included reviews by categorising their findings in the following framework, organised by timing of intervention (preconception, interconception and during pregnancy), and by intervention topic.

- Effective interventions: indicating that the review found high-quality evidence of effectiveness for an intervention.
- Possibly effective interventions (more evidence needed): indicating that the review found moderate-quality evidence of effectiveness for an intervention, but more evidence is needed.
- Ineffective interventions: indicating that the review found high-quality evidence of lack of effectiveness for an intervention.
- Probably ineffective interventions (more evidence needed): indicating that the review found moderate-quality evidence suggesting lack of effectiveness for an intervention, but more evidence is needed.
- No conclusions possible due to lack of evidence: indicating that the review found low- or very low-quality evidence, or insufficient evidence to comment on the effectiveness of an intervention.

The choice of category will reflect the information synthesised from the included reviews for the primary overview outcome (diagnosis of GDM). This approach to summarising the evidence is based on a Cochrane Overview of pain management in labour, which categorises interventions as "What works", "What may work", and "Insufficient evidence to make a judgement" (Jones 2012).
As part of the prepublication editorial process, four peers have commented on this protocol (an editor and three referees who are external to the editorial team), and the Group’s Statistical Adviser.

We acknowledge the support of the Pregnancy and Childbirth Editorial Group, the Australian and New Zealand Satellite of Cochrane Pregnancy and Childbirth (funded by the Australian National Health and Medical Research Council), and The Liggins Institute.

This project was supported by the National Institute for Health Research, via Cochrane Infrastructure funding to Cochrane Pregnancy and Childbirth. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

**REFERENCES**

**Additional references**

**Academy of Nutrition and Dietetics 2008**


**ACOG 2013**


**Adams 1998**


**Alkhafry 2013**


**Baillargeon 2010**


**Barakat 2012**


**Becker 2011**


**Berkowitz 1992**


**Boney 2005**


**Bourlon 1999**


**Buchanan 1990**


**Burton-Freeman 2000**


**Cai 2012**

Cai W, Ramdas M, Zhu L, Chen X, Striker GE, Vlassara H. Oral advanced glycation end products (AGEs) promote...

Calder 2006

Chiu 2004

Cho 2000

Danyliv 2014

Dang 2010

Davis 2005

Dempsey 2004

Dodd 2014

FAO/WHO 2001

Ferrara 2007

Fraser 1983

Fraser 1988

Interventions for preventing gestational diabetes mellitus: an overview of Cochrane Reviews (Protocol)
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
Interventions for preventing gestational diabetes mellitus: an overview of Cochrane Reviews (Protocol)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Gonzalez-Quintero 2007

Hanson 2015

He 2015

Health Service Executive Ireland 2010
Health Service Executive Ireland. Guidelines for the Management of Pre-Gestational and Gestational Diabetes from Pre-Conception to the Post-Natal Period. Dublin: Offices of the Nursing and Midwifery Services Director, 2010.

Hill 2014

Holt 2014

Jack 1990

Jackson 1987

Jenkins 2000

Jones 2012

Kantarzis 2009

Kazi 2015

Kennedy 1999

Khan 2013

Kim 2002

Knopp 1991

Knowler 2002

Kohrt 1993

Kondo 2010

Kris-Etherton 2000

Kris-Etherton 2009
Landon 2009

Langer 2005

Lardinois 1987

Larson-Meyer 2006

Ley 2011

Liese 2005

Lin 2012

Lindsay 2014

Ludwig 2002

Luoto 2011

Ma 2008

Magee 1990

Marcotorchino 2012

Markovic 2015

Mcintosh 2001

Metzger 2007

NICE 2010

NICE 2015

Norman 1980
Pan 1993

Perseghin 1996

Pole 1999

Rakhshani 2012

Reiser 1979

Rizzo 1991

Rogozinska 2015

Saltiel 1990

Setji 2005

Skupien 2014

Slocum 2002

Soheilykhah 2013

Solomon 1997

Soo 1999

Stafne 2012

Stumvoll 1995

Tannous dit El Khoury 2006

Theriault 2014
Thompson 2013

Tuomilehto 2001

Vahouny 1988

Viollet 2012

Whiting 2015

WHO 2013

Wijendran 1999

Wollen 1988

Xiong 2001

Yeung 2010

Yki-Jarvinen 1983

Zhang 2006

Zhang 2014

Zhou 2012

* Indicates the major publication for the study
Appendix 1. Prespecified outcomes for interventions for the prevention of GDM

Maternal outcomes
- GDM (as defined by systematic review authors)
- Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension and eclampsia)
- Mode of birth
- Induction of labour
- Perineal trauma
- Placental abruption
- Postpartum haemorrhage
- Postpartum infection
- Gestational weight gain
- Adherence to the intervention
- Behaviour changes associated with the intervention
- Relevant biomarker changes associated with the intervention (e.g. adiponectin, free fatty acids, triglycerides, high density lipoproteins, low density lipoproteins, insulin)
- Sense of well being and quality of life
- Views of the intervention
- Breastfeeding (e.g. at discharge, six weeks postpartum)

Maternal long-term outcomes
- Postnatal depression
- Postnatal weight retention or return to prepregnancy weight
- Body mass index (BMI)
- GDM in a subsequent pregnancy
- Type 1 diabetes
- Type 2 diabetes
- Impaired glucose tolerance
- Cardiovascular health (as defined by systematic review authors, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)

Neonatal/infant outcomes
- Large-for-gestational age
- Perinatal mortality (stillbirth and neonatal mortality)
- Mortality or morbidity composite
- Stillbirth
- Neonatal mortality
- Gestational age at birth
- Preterm birth (less than 37 weeks’ gestation and less than 32 weeks’ gestation)
- Apgar score (less than seven at five minutes)
- Macrosomia
- Small-for-gestational age
- Birthweight and z-score
- Head circumference and z-score
- Length and z-score
- Ponderal index
• Adiposity
• Shoulder dystocia
• Bone fracture
• Nerve palsy
• Respiratory distress syndrome
• Hypoglycaemia
• Hyperbilirubinaemia

Later infant and childhood outcomes
• Weight and z-scores
• Height and z-scores
• Head circumference and z-scores
• Adiposity (e.g. as measured by BMI, skinfold thickness)
• Blood pressure
• Type 1 diabetes
• Type 2 diabetes
• Impaired glucose tolerance
• Dyslipidaemia or metabolic syndrome
• Neurosensory disability
• Educational achievement

Child as an adult outcomes
• Weight
• Height
• Adiposity (e.g. as measured by BMI, skinfold thickness)
• Cardiovascular health (as defined by systematic review authors, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)
• Type 1 diabetes
• Type 2 diabetes
• Impaired glucose tolerance
• Employment, education and social status/achievement

Health service use outcomes
• Number of hospital or health professional visits (e.g. midwife, obstetrician, physician, dietitian, diabetic nurse)
• Number of antenatal visits or admissions
• Length of antenatal stay
• Length of postnatal stay (mother)
• Length of postnatal stay (baby)
• Costs to families associated with the management provided
• Costs associated with the intervention
• Cost of maternal care
• Cost of offspring care (including neonatal intensive care unit admission)
CONTRIBUTIONS OF AUTHORS
Caroline Crowther and Julie Brown had the original concept for the overview. Robyn Lawrence was responsible for writing the protocol. All authors provided review and feedback on the protocol drafts which were incorporated into the final version of the protocol.

DECLARATIONS OF INTEREST
Julie Brown, Emily Shepherd, Philippa Middleton and Caroline Crowther are authors of reviews that may be included in this overview. Should we identify such reviews, we will screen them for inclusion, using overview authors not involved in those particular reviews. If we include them, overview authors not involved in those particular reviews will extract data and conduct 'Risk of bias' assessments.
Robyn Lawrence receives a PhD scholarship from the University of Auckland. The overview will be included in Robyn's PhD but the scholarship is not specifically to complete the overview.
There are no other known conflicts of interest.

SOURCES OF SUPPORT

Internal sources
- The Liggins Institute, The University of Auckland, New Zealand.
- ARCH: Australian Research Centre for Health of Women and Babies, Robinson Research Institute, The University of Adelaide, Australia.

External sources
- National Health and Medical Research Council, Australia Funding for the PCG Australian and New Zealand Satellite, Australia.