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Interventions to prevent women developing gestational diabetes mellitus: an overview of Cochrane Reviews (Protocol)

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Interventions to prevent women developing gestational diabetes mellitus: an overview of Cochrane Reviews

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ABSTRACT

This is a protocol for a Cochrane Review (Overview). The objectives are as follows:

To summarise the evidence from Cochrane systematic reviews regarding the effects of interventions to prevent women developing gestational diabetes mellitus (GDM).

BACKGROUND

Description of the condition

Gestational diabetes mellitus (GDM) is glucose intolerance causing hyperglycaemia with onset during pregnancy. The optimal blood glucose concentration cut-off to diagnose GDM remains controversial (ACOG 2013; Cheung 2018; Coustan 2010; HAPO 2008; IADPSG 2010; Ministry of Health 2014; NICE 2015). Lower blood glucose concentration thresholds for diagnosis have resulted in more women being diagnosed with GDM (IADPSG 2010; Nankervis 2014; WHO 2013). The prevalence of GDM varies internationally with between 1% to 36% of pregnant women affected (Bottalico 2007; Egan 2017; Ferrara 2007; McIntyre 2018; Melchior 2017; NICE 2015). Prevalence varies by country, ethnicity and the diagnostic thresholds (Farrar 2016; HAPO 2008; Pu 2015).

Normal pregnancy is characterised by changes in the metabolism of carbohydrate, amino acids and lipids. The result of these combined changes is a switch to maternal use of lipids as a source of energy, sparing glucose and amino acids for the fetus. In the first trimester of pregnancy there is increased insulin sensitivity (Catalano 1991; Catalano 1992; Catalano 1993) as a result of adaptation of the pancreatic β-cells (Van Asche 1978), increased insulin synthesis (Weinhaus 1996) and secretion (Sorenson 1993), leading to improved utilisation and oxidation of glucose. By 14
weeks’ gestation, the first phase of insulin secretion in response to a glucose load has increased by approximately 120% (Bowes 1996; Catalano 1993), resulting in a reduced plasma glucose concentration (Catalano 1992). In the second and third trimesters, insulin sensitivity reduces (Catalano 1991; Catalano 1992; Catalano 1993; Ryan 1985) and hepatic gluconeogenesis increases (Nelson 1994).

In women with GDM, the increase in first phase insulin secretion in response to a glucose load is reduced (Catalano 1993), with inadequate adaptation of β-cells leading to impaired glucose homeostasis (Buchanan 2001). In the second and third trimesters the insulin sensitivity is further reduced (Catalano 1998) with resultant maternal hyperglycaemia, elevated glycated haemoglobin (HbA1c) concentrations and increased transport of glucose across the placenta to the developing fetus (Setji 2005). During normal pregnancy, changes in adipocytes result in more fat stores being laid down with increased synthesis and reduction in clearance of triglycerides (Ginci 1997), resulting in an increase in all plasma lipid components (Butte 2000). Women with GDM have hyperlipidaemia (raised levels of lipids in the blood) beyond that seen in normal pregnancy (Koukkou 1996) due to increased synthesis in the liver and reduced activity of lipoprotein lipase and hepatic lipase (Ginci 1997; Sattar 1997). Higher concentrations of free fatty acids cross the placenta than in normal pregnancy (Laqué 2011), which may contribute to the risk of macrosomia (large baby) (Knopp 1992).

There are multiple risk factors for GDM (Berkowitz 1992; Chu 2007; Khan 2013; Pu 2015; Solomon 1997; Theriault 2014; Xiong 2001). These include advanced maternal age, maternal high or low birthweight, high parity (Petry 2010), polycystic ovarian syndrome (Toulou 2009), a past history of GDM (Kim 2007), family history of first-degree relatives with GDM or type 2 diabetes (Petry 2010), maternal overweight or obesity (Morisset 2010; Torloni 2009), physical inactivity before or in early pregnancy (Dempsey 2004; Tobias 2011; Zhang 2014), gestational weight gain (Morisset 2010; and a past history of a macrosomic baby or a stillbirth (Petry 2010). Impaired glucose tolerance is common to many of these risk factors, but the exact mechanisms by which each contributes to the development of GDM are uncertain. Some of these risk factors are potentially modifiable through preventive interventions.

Women with GDM have a higher risk of pre-eclampsia and need for induction of labour (Dodd 2007). Women with a history of GDM have a greater than seven-fold increased risk of developing type 2 diabetes later, with more than half these women developing type 2 diabetes within 10 years after giving birth (Bellamy 2009; Kim 2002). Infants born to mothers with GDM are at increased risk of being born large-for-gestational age (Sacks 2015), and are therefore more likely to experience birth injuries such as nerve palsy, bone fracture and shoulder dystocia. In the neonatal period, they are at higher risk of respiratory distress syndrome, jaundice and hypoglycaemia (reduced levels of blood sugar) (Adams 1998; Crowther 2005; Gonzalez-Quintero 2007; He 2015; Landon 2009; Langer 2005). Longer-term health consequences into childhood and adulthood include obesity, diabetes, the metabolic syndrome (Boney 2005; Choo 2000), and adverse neurodevelopmental outcomes (Chatzi 2014; Fraser 2012; Nelson 2000; Torres-Espinola 2015).

Description of the interventions

Interventions to prevent GDM have been used preconception, during pregnancy and interconception. Preconception and interconception interventions have been used, particularly in women at high risk of GDM, such as those who are overweight or obese (Yeung 2010), or with a history of GDM (Khan 2013; Shyam 2013). The opportunity exists to intervene with health promotion strategies prior to and between pregnancies for women identified with risk factors for GDM (Hanson 2015; Jack 1990).

Interventions directed at preventing GDM include dietary or exercise interventions or a combination of these, dietary supplement interventions and pharmaceutical interventions.

The focus of some dietary advice interventions for GDM prevention have been specific, such as increasing fibre intake (Fraser 1983; Fraser 1988) or aiming for a low glycaemic index diet (Kizirian 2017; Markovic 2015). Others have included broader advice regarding “healthy eating” as part of more comprehensive lifestyle interventions (Quinlivan 2011).

Exercise or physical activity interventions for preventing GDM have varied from general advice to specific individualised programmes using a range of different activities, such as aerobic activities, stationary cycling or yoga (Barakat 2012; Guelfi 2016; Ong 2009; Rakhshani 2012; Stafne 2012). These have been employed in isolation (Barakat 2012; da Silva 2017; Goodarzi-Khoigani 2017; Guelfi 2016; Ong 2009; Stafne 2012), or in combination with dietary interventions (Dodd 2014; Harrison 2013; Koivusalo 2016; Luoto 2011; Petteella 2014; Poston 2015; Simmons 2015).

Dietary supplement interventions such as probiotics (Lindsay 2014; Luoto 2010; Wickens 2017), myo-inositol (D’Anna 2013; Fanren 2017; Santamaria 2016), vitamin D (Bao 2017; Soheilkhah 2013) and fish oils have been investigated for GDM prevention (Zhou 2012).

Pharmaceutical therapies, which may have a role in GDM prevention, include sulphonylureas, biguanides, thiazolidinediones, alpha-glucosidase inhibitors, meglitinides and peptide analogues. Metformin or glibenclamide (also known as glyburide) are the only oral hypoglycaemics recommended in clinical practice guidelines for use in pregnancy (ACOG 2013; NICE 2015). However, there is a paucity of data regarding the safety of many of these in pregnancy (Holt 2014; Kavitha 2013; Slocum 2002). Where safety data are available, this has often been limited to short-term health outcomes. The MiG trial investigated the use of metformin for women with GDM, and demonstrated metformin was safe in the offspring, at least up to two years of age (Rowan 2011).
**How the intervention might work**

**Dietary interventions**

Different dietary components have direct and indirect effects on glycaemic profile. Interventions that alter these could be utilised to reduce GDM risk (Ley 2011; Rogozinska 2015; Zhang 2006). Insulin sensitivity and secretion are reduced in association with high simple sugar intake (Davis 2005; Reiser 1979). With ongoing high sugar intake, pancreatic exhaustion may ensue with impaired glucose tolerance (Ludwig 2002). Less insulin resistance is seen with a high-fibre and low-glycaemic index diet. Fibre slows digestion (Burton-Freeman 2000; Jenkins 2000; Vahlouny 1988) and rate of glucose absorption, thus altering the blood glucose concentration and insulin response (Jenkins 2000; Liese 2005; McIntosh 2001). Increasing dietary fibre intake may reduce appetite and hence insulin resistance associated with adiposity (Burton-Freeman 2000). Intake of protein and fats may also reduce appetite (Tannous dit El Khoury 2006) with similar effect (Kantartzis 2009; Kohrt 1993; Pan 1993) and through protection of β-cells from oxidative injury (Cai 2012; Lin 2012). A general reduction in calorie intake with resultant weight loss and reduced adiposity improves insulin sensitivity and glycaemic profile (Knopp 1991; Larson-Meyer 2006). This needs to balanced against potential risks of weight loss during pregnancy such as ketonaemia associated with marked calorie restriction (Churchill 1969; Magee 1990; Metzger 2007; Ornoy 1998; Rizzo 1991). Due to these concerns, international guidelines do not recommend hypocaloric diets during pregnancy (Ireland 2010; NICE 2010; Thompson 2013). There is ongoing debate as to whether caloric restriction might be appropriate in overweight and obese pregnant women (Knopp 1991; Procter 2014). Interventions to aid with weight loss in overweight or obese women preconception or interconception may reduce the risk of GDM in any future pregnancy (Pole 1999).

**Exercise interventions**

The risk of developing GDM is inversely associated with the amount of regular physical activity before or during pregnancy (Dempsey 2004; Zhang 2014). There is increased energy expenditure and hence glucose consumption during exercise; blood flow through muscle mass and capillary surface area for glucose exchange increases (Rose 2005; Sjøberg 2011). During muscle contraction, there is translocation of the glucose transporter type 4 (GLUT-4) from within skeletal muscle cells to the surface (Jessen 2005; Kennedy 1999; Rose 2005) with resultant increased glucose uptake. The increase in insulin sensitivity continues beyond the exercise period (Jensen 2012; Perseghin 1996). Muscle mass increases with regular physical activity, and thus glucose tolerance and insulin sensitivity are likely to improve (Yki-Jarvinen 1983).

**Diet and exercise interventions combined**

Combined interventions targeting more than one of the multiple risk factors for GDM could be synergistic. Prevention of type 2 diabetes has been demonstrated using combined dietary, exercise and weight loss interventions (Haw 2017; Knowler 2002; Tuomilehto 2001). These might be expected to have a similar effect in prevention of GDM.

**Dietary supplement interventions**

**Probiotics**

Probiotic use can change the microbiome of the gut, which may reduce insulin resistance (FAO/WHO 2001; Hill 2014; Kondo 2010), through decreasing inflammatory signalling (Ma 2008) and upregulating genes involved in fat metabolism and insulin sensitivity (Kondo 2010).

**Myo-inositol**

Myo-inositol, a polyol with insulin-mimetic properties (Croze 2013; Saltiel 1990) involved in insulin transduction signalling (Baillargeon 2010), increases GLUT-4 translocation to the cell membrane in skeletal muscle (Dang 2010), thus improving insulin sensitivity (Corrado 2011). Supplementary use in polycystic ovarian syndrome results in reduced fasting insulin concentrations (Unfer 2017). Myo-inositol is present in the diet in some seeds, grains, nuts, beans, vegetables and fruit (Clements 1980).

**Vitamin D**

Vitamin D deficiency is associated with insulin resistance (Esteghamati 2014) and poor pancreatic β-cell function (Chiu 2004). 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). Vitamin D deficiency may reduce pancreatic insulin secretion (Bourlon 1999; Norman 1980), while supplementation with vitamin D may influence the expression of insulin-sensitive genes (Alkharfy 2013), thus reducing inflammatory markers and improving glucose uptake (Marcotorchino 2012).

**Fish oil**

The circulating concentrations of several long-chain polyunsaturated fatty acids are altered in GDM (Wijendran 1999). Omega-3 fatty acids have several anti-inflammatory effects (Calder 2006). The predominant sources of the omega-3 fatty acids, eicosapentaenoic acid and docosahexaenoic acid, are fish and fish oils (Kris-Etherton 2000; Kris-Etherton 2009). The lipid composition of cell membranes is altered with changes to dietary fatty acid
composition (Calder 2006; Lardinois 1987), which affects insulin binding and sensitivity. Increased insulin secretion and sensitivity may result from omega-3 or fish oil supplementation (Baynes 2018). Increased inflammation can result in insulin resistance, while omega-3 fatty acids inhibit TLR-2 and TLR-4 receptors for inflammatory cytokines (Lee 2004).

**Pharmaceutical interventions**

Metformin, a biguanide, crosses the placenta with similar concentrations found in maternal and fetal circulations (Vanky 2005). Metformin reduces hepatic gluconeogenesis (Stumvoll 1995; Wollen 1988), and enhances peripheral glucose uptake and utilisation (Viollet 2012) improving insulin sensitivity and reducing hyperglycaemia (Jackson 1987). Metformin may enhance insulin sensitivity and preserve pancreatic β-cell capacity in women with polycystic ovarian syndrome (Ainuddin 2015). Glibenclamide crosses the placenta with fetal blood concentrations approximately 70% of maternal blood concentrations (Hebert 2009). Glibenclamide stimulates insulin secretion, but has been associated with an increased risk of macrosomia, neonatal hypoglycaemia and higher maternal weight gain in comparison to metformin (Liang 2017).

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

A number of risk factors for GDM, such as physical inactivity, being overweight or obese prior to pregnancy, and having a poor diet are potentially modifiable. While different strategies have shown promise in the prevention of GDM, it is currently unclear which strategies are most 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, and pregnant women at risk of developing GDM, and their families. Use of the overview to identify and target effective preventive interventions may contribute to reducing the increase in rates of GDM seen globally as well as reducing the significant short- and long-term health risks for the mothers and their infants. Further, this overview may identify areas requiring further priority research.

**OBJECTIVES**

To summarise the evidence from Cochrane systematic reviews regarding the effects of interventions to prevent women developing gestational diabetes mellitus (GDM).

**METHODS**

**Criteria for considering reviews for inclusion**

In this overview of systematic reviews, we will include only published Cochrane systematic reviews, that assess interventions that may prevent gestational diabetes mellitus (GDM), reporting GDM as a primary or secondary outcome of the review. Cochrane protocols and titles will be identified for potential future inclusion in an update of the overview, and classified as ‘ongoing reviews’ (in an Appendix).

If a review identified for inclusion is more than two years out of date, we will contact the Cochrane Pregnancy and Childbirth Editorial Base to identify whether an update is in progress. We will not contact individual review authors. If such a review is out of date and will not be updated in time to be included in the overview, we will include the last published version and acknowledge this as a potential limitation.

**Participants**

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

**Interventions**

We will include interventions prior to pregnancy (preconception), between pregnancies (interconception), or implemented prior to GDM screening in pregnancy, and for each of these time periods these may include:

- dietary interventions;
- exercise interventions;
- dietary and exercise interventions combined;
- dietary supplement interventions (e.g. probiotics, myo-inositol, vitamin D and omega-3 fatty acids);
- pharmaceutical interventions (e.g. oral anti-diabetic pharmaceutical therapies).

We will include reviews comparing the above interventions with standard care or no intervention (or a placebo), as well as those comparing different interventions.

**Outcome**

- Gestational diabetes mellitus (GDM) (defined by review authors and trialists).

**Search methods for identification of reviews**

We will search the Cochrane Database of Systematic Reviews using key words ‘gestational diabetes’ OR ‘GDM’. We will use the search terms to search ‘all text’, and not limited to ‘title, abstract, or
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 Review of Interventions (Higgins 2011).

Selection of reviews

Two overview authors will independently assess for potential inclusion all Cochrane systematic reviews we identify that evaluate the effects of the aforementioned interventions and report on the incidence of GDM. We will resolve any disagreement through discussion or 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 discussion with a third overview author. If any information from the reviews is missing, we will access the published papers of the individual study or 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, and their characteristics.
- Risk of bias of the included trials (as reported by the review authors; see ‘Risk of bias of included studies within reviews’ below, under Assessment of methodological quality of included reviews).
- Interventions and comparisons relevant to this overview.
- The prespecified outcome relevant to this overview as listed above.
- Any other characteristics required to assess and report on review quality (see ‘Quality of included reviews’ under Assessment of methodological quality of included reviews).

Statistical summaries

- The summary intervention effects, including the pooled effects (e.g. risk ratios (RRs), odds ratios (ORs), mean differences (MDs)), 95% confidence intervals (CIs), and numbers of studies and participants contributing data to each pooled effect from comparisons and for outcomes relevant to this review.
- Results of any subgroup or sensitivity analyses conducted by the authors for our primary outcome.
- 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).
- We will conduct a sensitivity analysis excluding Cochrane systematic reviews with a ROBIS (Risk of Bias in Systematic reviews) review rating that is of high concern for risk of bias in any domain.

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 outcome.

Assessment of methodological quality of included reviews

Quality of included reviews

We will assess the methodological quality of each systematic review using the ROBIS tool (Whiting 2015). The ROBIS tool assesses 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.

Two overview authors will independently assess the quality of the included reviews using ROBIS, and another overview author will verify this assessment. We will resolve differences through discussion or, if needed, through discussion with a third overview author.

Quality of evidence in the included reviews

We will assess the quality of the evidence for our primary outcome using GRADE. 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.

Interventions to prevent women developing gestational diabetes mellitus: an overview of Cochrane Reviews (Protocol)
• 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 the review for each intervention, timing of intervention (preconception, interconception and during pregnancy) and whether GDM was a primary or secondary outcome.

Risk of bias of included studies within reviews
We will not reassess the risk of bias of included studies within reviews, but instead will report study risk of bias 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 risk of bias. We will collect this information during the data extraction process.

Data synthesis
We will undertake a narrative description of the included Cochrane systematic reviews. We will not examine indirect comparisons or 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 focus/topic. We will assign graphic icons to communicate the direction of review effect estimates and our confidence in the available data. This is the framework adopted by Medley and colleagues in their overview on ‘Interventions during pregnancy to prevent preterm birth: an overview of Cochrane systematic reviews’, (Medley 2018), and was based on graphics produced by the WHO to describe different types of workers and their roles in maternal and newborn care (http://optimizemnh.org/optimizing-health-worker-roles-maternal-newborn-health/). We will also use graphic icons to indicate mutually exclusive assessment categories:
• Clear evidence of benefit (MODERATE or HIGH quality evidence)
• Clear evidence of harm (MODERATE or HIGH quality evidence)
• Clear evidence of no effect or equivalence (MODERATE or HIGH quality evidence with narrow confidence intervals crossing the line of no effect)
• Possible benefit (LOW quality evidence with clear benefit, or MODERATE or HIGH quality evidence with wide confidence interval)
• Possible harm (LOW quality evidence with clear harm, or MODERATE or HIGH quality evidence with wide confidence interval)
• Unknown benefit or harm (LOW quality evidence with wide confidence interval or VERY LOW quality evidence)

The choice of category will reflect the information synthesised from the included reviews for the overview outcome (GDM). We will use separate assessments for different comparisons when required (e.g. where one intervention was compared with both placebo (or no treatment) and with an alternative intervention). This approach to summarising the evidence is based on an earlier overview ‘Antenatal and intrapartum interventions for preventing cerebral palsy: an overview of Cochrane systematic reviews’ (Shepherd 2017).

ACKNOWLEDGEMENTS
The previous version of this protocol (Lawrence 2016) was commented on by an editor, three peer referees 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, and The Liggins Institute.

This protocol 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.

Robyn Lawrence with colleagues Julie Brown, Philippa Middleton, Emily Shepherd, Stephen Brown and Caroline Crowther in 2016 prepared a protocol for an overview entitled ‘Interventions for preventing gestational diabetes mellitus: an overview of Cochrane Reviews,’ (Lawrence 2016). This protocol has now been amended. Robyn Lawrence and Julie Brown have stepped down from the
We would like to thank Robyn and Julie for their contribution to the original protocol.

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References to other published versions of this review

Lawrence 2016
WHAT'S NEW

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<th>Date</th>
<th>Event</th>
<th>Description</th>
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| 30 April 2019 | New citation required and major changes | The author team have changed to include a new lead author, Rebecca Griffith. Julie Brown and Robyn Lawrence have stepped down from the team. The title has changed slightly from, "Interventions for preventing gestational diabetes mellitus: an overview of Cochrane Reviews", to "Interventions to prevent women developing gestational diabetes: an overview of Cochrane Reviews"  
The scope has also changed, as outlined below.  
Description of the condition: expanded to provide a description of the metabolic changes that take place in a normal versus gestational diabetes mellitus (GDM) pregnancy  
Description of the interventions: additional recent references added to update  
Outcomes: as the aim of the overview is to summarise the evidence relating to the prevention of GDM, the primary outcome is prevention of GDM  
Statistical summaries: subgroup and sensitivity analyses added  
Data synthesis: the framework has changed to improve presentation and readability |
| 30 April 2019 | Amended                        | The original protocol published in 2016 (Lawrence 2016) has been amended to reflect a change in scope.                                                                                                                                                                                                                                                   |

CONTRIBUTIONS OF AUTHORS

Caroline Crowther and Julie Brown had the original concept for an overview of interventions to prevent women developing GDM. Rebecca Griffith wrote the first draft of this new protocol. All authors provided review and feedback on the draft versions of the protocol and agreed on the final version published.

DECLARATIONS OF INTEREST

Rebecca Griffith receives a Clinical Research Training Fellowship award from the Health Research Council of New Zealand. The overview will be included in Rebecca's PhD, but the award is not specifically to complete the overview. There are no other known conflicts of interest.

Abigail E Moore: none known.

Jane Alsweiler is on the steering committee for a randomised controlled trial of tight glycaemic targets for women with gestational diabetes.

Emily Shepherd, Philippa Middleton, Jane Alsweiler 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 Cochrane systematic reviews will assess eligibility, extract data and
GRADE outcomes, if not already undertaken by the review authors.

Stephen Brown: none known.

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