Optimal treatments and experiences for women with gestational diabetes mellitus (GDM): improving health for mothers and babies

Ruth Martis

A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy (PhD) - Health Sciences, The University of Auckland, 2018.

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Abstract

Aims: To provide insights into optimal treatments, glycaemic targets, and experiences of women with gestational diabetes mellitus (GDM) to guide clinical management.

Optimal treatments for women with GDM

Method: An overview of Cochrane systematic reviews to synthesise evidence on treatments for women with GDM.

Findings: Eight systematic reviews were eligible and included a total of 62 randomised trials involving 9133 women, 8373 babies and 767 children. High-quality evidence suggested that lifestyle interventions were ineffective for reducing the likelihood of induction of labour compared with usual diet/diet alone. Exercise compared with control was ineffective in improving the return to pre-pregnancy weight. No other high-quality evidence was found.

Promising interventions included lifestyle interventions (reduced risk of large for gestational age) and the DASH diet (reduced rate of caesarean section).

Glycaemic treatment targets for women with GDM

Method: A Cochrane systematic review to synthesise evidence from randomised controlled trials on the effect of different glycaemic targets for women with GDM and their children.

Findings: One randomised trial with 180 women was eligible and included. Based on limited data it remains unclear which glycaemic targets to recommend for women with GDM for improving their health and that of their babies.

Views, experiences, barriers, and enablers of women with GDM on achieving optimal glycaemic control

Methods: Sixty women with GDM completed the survey and semi-structured interview.

Findings: The survey highlighted how the 60 women viewed adherence to their glycaemic targets and identified ten enablers and nine barriers. Thematic analysis using the Theoretical Domains Framework from the semi-structured interviews provided insights of the women's first reaction to a diagnosis of GDM and identified multiple barriers and enablers for women with GDM trying to achieve optimal glycaemic control within ten relevant Theoretical Domains.

Conclusions

This thesis found limited evidence for effective treatments and glycaemic targets for women with GDM. A need for high-quality research with long-term follow-up was identified. Women with GDM in New Zealand identified multiple enablers and barriers to achieving optimal glycaemic control that need to be considered when providing health care.

Dedication

This thesis is dedicated to all women with GDM and their babies.

Acknowledgements

It has been said *it takes a village to raise a child.* This African proverb means that it takes an entire community to raise a child. I would like to extend this saying to *it takes a whole community to complete a PhD thesis.*

I would like to thank everyone that helped me throughout this study. If it were not for your support, encouragement and advice, this thesis would not have been completed. Please accept my heartfelt thanks and know that I really could not have done it without you. I am unable to name everyone here but would like to mention a few especially.

I would like to thank the 60 women who participated in the studies. The enthusiasm shown during the interviews and the survey was appreciated and highlighted the importance to have their voices heard.

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List of Abbreviations

ACOG	American College of Obstetricians and Gynecologists
ADA	American Diabetes Association
ADHB	Auckland District Health Board
ADHD	Attention Deficit Hyperactivity Disorder
ADIPS	Australasian Diabetes in Pregnancy Society
AMSTAR	Assessment of Multiple Systematic Reviews
ASD	Autism Spectrum Disorder
BMI	Body Mass Index
CBG	Capillary Blood Glucose
CDA	Canadian Diabetes Association
DASH	Dietary Approaches to Stop Hypertension
DHB	District Health Board
DSES	Diabetes Self-Efficacy Scale
DSME	Diabetes Self-Management Education
DSMS	Diabetes Self-Management Support
EASD	European Association for the Study of Diabetes
FPG	Fasting Plasma Glucose
GDM	Gestational Diabetes Mellitus
GDNO	Gestational Dysglycaemia of Nutritional Origin
GLUT	Glucose Transporters
GPP	Good Practice Point
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HAPO	Hyperglycaemia and Adverse Pregnancy Outcomes
HCS	Human Chorionic Somatomammotropin
HDEC	Health and Disability Ethics committee
IADPSG	International Association of the Diabetes and Pregnancy Study Groups
IOL	Induction of Labour
LGA	Large for Gestational Age

LMC	Lead Maternity Carer
NICE	National Institute for Health and Care Excellence
NZSSD	New Zealand Society for the Study of Diabetes
OGCT	Oral Glucose Challenge Test
OGTT	Oral Glucose Tolerance Test
OHA	Oral Hypoglycaemic Agents
PRIG	Pregnancy Related Intolerance to Glucose
ROBIS	Risk of Bias in Systematic Reviews
SGA	Small for Gestational Age
SIGN	Scottish Intercollegiate Guidelines Network
TDF	Theoretical Domains Framework
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
TNF-α	TNF tumour necrosis factor-alpha
WHO	World Health Organisation

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Chapter 2 - Cochrane Overview Review: Treatments for women with GDM

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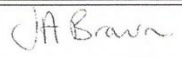
J Brown		10/10/17

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Chapter 3 - Cochrane Systematic Review:

Different intensities for glycaemic control for women with GDM

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Chapter 4 - Quantitative study: Views and experiences of New Zealand women with GDM in achieving glycaemic control targets.

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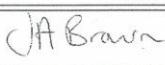
Julie Brown		12/10/17
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Nature of contribution by PhD candidate	Involved in conceiving the idea for the study, prepared the protocol, developed the interview guide, recruited 60 women, conducted the interviews, led the analysis, coded and classified the data, revised and synthesised the data into final domains and prepared the first draft of the manuscript and subsequent drafts. Wrote the first full draft version of the article. Incoporated feedback for all drafts and produced the final version.
Extent of contribution by PhD candidate (%)	90%

CO-AUTHORS

Name	Nature of Contribution
Julie Brown	Involved in conceiving the idea for the study. Contributed to the study design, project administration, coded and classified the data with RM, revised and synthesised the text into final domains with RM and commented on drafts of the manuscript and approved the final version of the article.
Judith McAra-Couper	Commented on drafts of the manuscript and approved the final version of the article.
Caroline A Crowther	Involved in conceiving the idea for the study. Contributed to the study design, project adminstration, thematic interpretation and commented on drafts of the manuscript and approved the final version of the article.

Certification by Co-Authors

The undersigned hereby certify that:

- the above statement correctly reflects the nature and extent of the PhD candidate's contribution to this work, and the nature of the contribution of each of the co-authors; and
- that the candidate wrote all or the majority of the text.

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Last updated: 19 October 2015

Chapter 1: Orientation to the studies

1.1 Introduction

The worldwide prevalence of gestational diabetes mellitus (GDM) is increasing and has been documented with variations between 5.2% to 31.6% depending on the ethnicity of the population and diagnostic criteria used (Cheung 2003; Ferrara 2007; Boyadzhieva 2012; Sacks 2012; Tran 2013; NICE 2015; Melchior 2017).

In 2015, 58,957 women in New Zealand gave birth (Ministry of Health 2017) and 9% were diagnosed with GDM. This has been reported as one in every 11 pregnant women being diagnosed with GDM (ADHB 2016). The incidence of GDM for pregnant women was higher in Indian (16%), Asian (15%), Pacific peoples (8%) compared to European (5%) and Māori (4.5%) (ADHB 2016). Maternal hyperglycaemia, associated with GDM, is a serious complication of pregnancy and a strong predictor for future type 2 diabetes mellitus (T2DM) (IADPSG 2010; ADHB 2016; Jowitt 2016). Given the prevalence, effective interventions for treatments for women with GDM for reducing adverse maternal and infant health outcomes are imperative.

1.2 Definition of gestational diabetes mellitus (GDM)

Gestational diabetes mellitus (GDM) is a medical condition that usually occurs in the second half of the pregnancy (Holt 2014). The World Health Organization defines GDM as a 'carbohydrate intolerance resulting in hyperglycaemia or any degree of glucose intolerance with onset or first recognition during pregnancy, usually from 24 weeks gestation onwards', (WHO 2013, p. 20) and resolves following the birth of the baby (Kampmann 2015). This definition excludes women with previously undiagnosed pre-existing type 1 (T1DM), type 2 diabetes (T2DM) or other form of diabetes first detected during screening earlier in pregnancy (Nankervis 2014; ADA 2017).

1.3 Pathophysiology of GDM

The continuous supply of appropriate and balanced nutrients from the pregnant woman to the fetus is essential for optimal health and growth. Glucose is the primary energy substrate for the fetus. Fetal glucose production is minimal and is dependent on placental supply of glucose from the maternal circulation, the key transporter being glucose transporters (GLUT) (Lager 2012). The regulation of fetal glucose metabolism requires the maintenance of maternal glucose concentration through increasing

maternal glucose production and at the same time developing maternal glucose intolerance and insulin resistance (Wilcox 2005). GLUTs transfer glucose to the fetus across the placenta for the production of fetal insulin and uptake of glucose into adipose tissue and skeletal muscle. The maternal-fetal gradient for transfer of glucose favours the fetus (Suman Rao 2013), that would result in the transport of high concentrations of glucose to the fetus in the case of severe and prolonged maternal hyperglycaemia.

1.3.1 Insulin resistance in pregnancy

Insulin, a peptide hormone secreted by the β cells of the pancreatic islets of Langerhans, maintains normal blood glucose levels by facilitating cellular glucose uptake, regulating carbohydrate, lipid, and protein metabolism, and promoting cell division and growth through its mitogenic effects (Wilcox 2005). Either inadequate insulin secretion, such as in T1DM, or insulin resistance (such as in T2DM or GDM), defined as insulin acting less effectively in promoting glucose uptake, such as in T2DM or GDM, can result in hyperglycaemia (Devlieger 2008; Petry 2010). Insulin resistance increases with advancing gestation (Catalano 2014). Late in pregnancy insulin sensitivity falls by about 50% (Di Cianni 2003; Lain 2007). It is believed that this is a normal physiologic response ensuring that the growing fetus receives sufficient glucose and other nutrients. At this point, maternal insulin resistance may occur as the pregnant woman cannot compensate with the increased demand for insulin (Ragnarsdottir 2010; McCance 2011).

1.3.2 Contributors to insulin resistance

The two main contributors to insulin resistance are increased maternal adiposity and the insulin desensitizing effects of hormones produced by the placenta (Lapolla 2005). GDM usually resolves following the birth, with insulin resistance decreasing rapidly postnatally (Hare 2014). This rapid decrease suggests that the major contributors to insulin resistance are the placental hormones, including tumour necrosis factor-alpha (TNF-α), placental lactogen, placental growth hormone human chorionic somatomammotropin (HCS), cortisol, oestrogen, and progesterone (Devlieger 2008; NICE 2015). HCS stimulates pancreatic secretion of insulin in the fetus and inhibits peripheral uptake of glucose in the mother (Lapolla 2005). As the placenta grows during pregnancy, so does the production of the placental hormones, leading to a more insulin-resistant state (Evans 2009). If the pregnant woman's metabolic processes cannot compensate adequately, maternal hyperglycaemia results. In the literature several risk factors for developing GDM have been identified.

1.4 Risk factors for developing GDM

Recognised non-modifiable risk factors for pregnant women to develop GDM include advanced maternal age (Morisset 2010), specific ethnicities such as Asian, African American, Native American, Hispanic, and Pacific Island women (Carolan 2012a; Schneider 2012; Chamberlain 2013; Kim 2013), a family history of diabetes mellitus (Anand 2017), maternal high or low birthweight, polycystic ovarian syndrome (Cypryk 2008; Petry 2010), a history of having a previous macrosomic infant (birthweight 4000 grams or more) (Oster 2009; Zhang 2010) and a previous history of GDM (Ehrlich 2011).

Modifiable risk factors for pregnant women to develop GDM include maternal overweight (body mass index (BMI) equal to or greater than 25 kg/m^2) or obesity (equal to or greater than 30 kg/m^2) (Rosenberg 2005; Athukorala 2010; Kim 2010), physical inactivity (Chasan-Taber 2008), having a low-fibre and high-glycaemic load diet (Zhang 2006), and excessive weight gain during pregnancy, especially for those who are already overweight or obese (Hedderson 2010). It has been reported in the literature that the risk of developing GDM for pregnant women is 2.14-fold higher in overweight pregnant women, 3.56-fold higher in obese pregnant women, and 8.56-fold higher in severely obese pregnant women compared to pregnant women with a normal weight (Chu 2007; Mitanchez 2015a).

The New Zealand Health Survey, for the years 2011-2013, 'Understanding excess body weight' identified that six percent of women had an BMI of ≥40 kg/m2 (considered morbidly obese) with a steep increase in the morbid obesity rate in the 25 to 34-year-old age group, the period of active child bearing. Pacific adults were five times as likely to be extremely obese as non-Pacific adults. All ethnic groups had higher rates of extreme obesity among women compared to men; 21 percent of Pacific, 12 percent of Māori and four percent of European/other females were extremely obese (Ministry of Health 2015b) (Table 1.1). These results are concerning and identify factors for increased maternal and infant health risks.

Table 1.1: Body mass index/waist circumference ratio - adults

Classification by BMI	Waist circumference		
	Normal (< 94 cm in males, < 80 cm in females)	**High** (94–101 cm in males, 80–87 cm in females)	**Very high** (≥ 102 cm in males, ≥ 88 cm in females)
Underweight (< 18.5 kg/m^2)	Underweight (not applicable)	Underweight (not applicable)	Underweight (not applicable)
Healthy weight (18.5–24.9 kg/m^2)	No increased risk	No increased risk	Increased risk
Overweight (25.0–29.9 kg/m^2)	No increased risk	Increased risk	High risk
Obese1 (30.0–39.9 kg/m^2)	Increased risk	High risk	Very high risk
Extremely obese (≥ 40.0 kg/m^2)	Very high risk	Very high risk	Very high risk

Source: adapted from Ministry of Health 2015b

1.5 Maternal and infant health risks from GDM

There are a wide range of known short- and long-term health implications for the woman and her baby (Crowther 2005; Harder 2009; Landon 2009; Nolan 2011; Nankervis 2014; NICE 2015).

1.5.1 Maternal health risks from GDM

For women with GDM, the health risks include a higher risk of developing gestational hypertension and/or pre-eclampsia during her pregnancy, having an increased risk of induction of labour (IOL), preterm birth, caesarean section, perineal trauma, and postpartum haemorrhage (Crowther 2005; HAPO 2008; McCance 2011; NICE 2015). Evidence from published cohort studies indicates an increased risk of postpartum depression (Kozhimannil 2009; Nicklas 2013). Significant long-term risks from GDM include developing cardiovascular and metabolic disease (Garrison 2015; Wahlberg 2016) and half of the women with GDM are at risk of developing T2DM within five to 10 years, with up to a seven-fold increase in the risk of T2DM compared to normoglycemic pregnancies (Bellamy 2009; Rayanagoudar 2016).

1.5.2 Infant health risks from GDM

Health implications for the baby born to a mother who had GDM include an increased risk of being born macrosomic or large for gestational age (LGA) (Ornoy 2005; Koyanagi 2013; Young 2013; Wahlberg 2016), birth trauma that includes shoulder dystocia, bone fractures and nerve palsy (Athukorala 2010),

hyperbilirubinemia (Hedderson 2006; Mitanchez 2015b), respiratory distress syndrome (Landon 2009) and neonatal hypoglycaemia (Devlieger 2008; HAPO 2008; Harris 2013). Neonatal hypoglycaemia may be associated with developmental delay in childhood (Lucas 1988; Ornoy 2015). Long-term health risks include higher rates of obesity, development of T2DM in childhood (Page 2014) and in adulthood, hypertension, and cardiovascular disease (Ornoy 2011). Observational studies of children whose mothers had diabetes, including women with GDM, reported a higher rate of neurosensory disability, including gross and fine motor abnormalities, attention deficit hyperactivity disorder (ADHD), learning and language difficulties, and possibly autism spectrum disorder (ASD) (Gardener 2009; Krakowiak 2012; Nomura 2012; Abou-Elsaad 2017). Given the associated health risks from GDM, appropriate screening diagnosis and provision of appropriate treatment for GDM is an important global public health issue, with high-quality evidence needed for policy and practice decisions.

1.6 Screening and diagnosis for GDM

1.6.1 Screening and diagnosis of GDM internationally

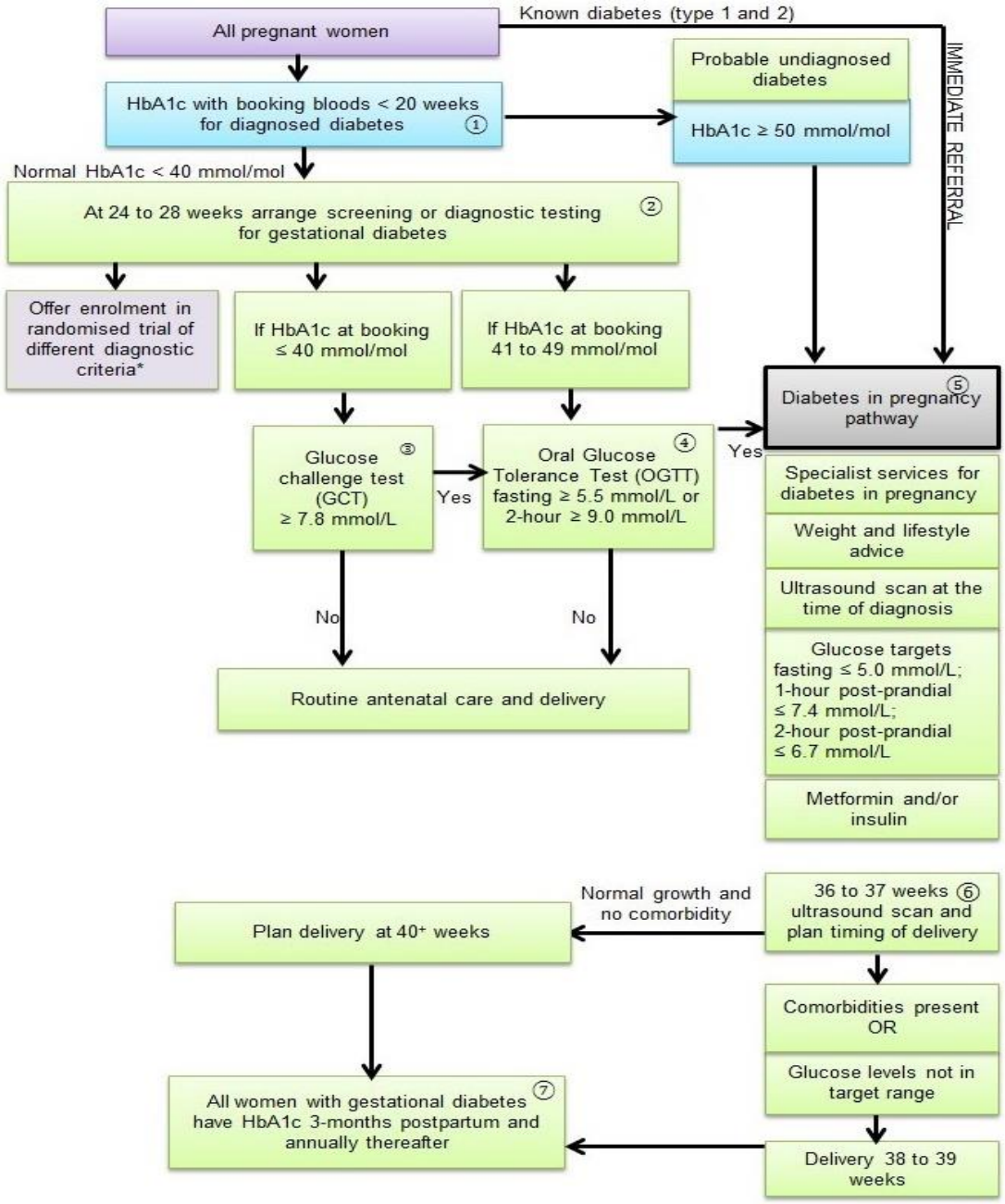
Screening for GDM aims to achieve an early diagnosis for treatment to start as soon as possible (Tieu 2017). Recommendations regarding screening for GDM and diagnostic criteria vary internationally (Tran 2013) with several screening and diagnostic tests being used to identify hyperglycaemia during pregnancy (IADPSG 2010; WHO 2013; Nankervis 2014; NICE 2015; Hughes 2016; ADA 2017; Hannah 2017).

1.6.2 Screening and diagnosis of GDM in New Zealand

In 2014 the New Zealand Ministry of Health published a national clinical practice guideline ‘Screening, Diagnosis and Management of Gestational Diabetes in New Zealand’. The guideline attempted to provide evidence-based recommendations for the diagnosis of previously undiagnosed diabetes in early pregnancy and of GDM mid-trimester (Ministry of Health 2014). The guideline recommends that all pregnant women be tested for haemoglobin A1c (HbA1c) concentrations, also known as glycated haemoglobin) at < 20 weeks of pregnancy (usually at the first antenatal booking) to exclude undiagnosed pre-existing diabetes (Ministry of Health 2014) (Figure 1.1). Further guidance recommends that between 24-28 weeks of pregnancy women undertake either a Glucose Challenge Test (GCT, also known as Polycose test), when the HbA1c results were normal, or a diagnostic Oral Glucose Tolerance Test (OGTT) when the HbA1c results were between 41 and 49 mmol/mol and a previous history of GDM

(Figure 1.1). The recommended New Zealand OGTT thresholds of fasting plasma glucose (FPG) ≥ 5.5 mmol/l (99 mg/dl) and 2-h post prandial plasma glucose ≥ 9.0 mmol/l (162 mg/dl) differ from the international recommendations for diagnostic thresholds (IADPSG 2010; WHO 2013). The guideline identified that robust evidence was needed for screening and diagnosing GDM (Ministry of Health 2014).

Figure 1.1: Flow chart of screening and diagnostic recommendations for diabetes in pregnancy in New Zealand



Source: adapted from Ministry of Health 2014, p. xiii

1.7 Treatment options for women with GDM

Women with GDM and health professionals providing care for women with GDM want to know which treatments are effective in achieving optimal glycaemic control and reduce short- and long-term risks of GDM (Farrar 2017). There are multiple recommended interventions in the literature, which include different diets, a range of physical exercise advice, lifestyle interventions and pharmacological hypoglycaemic agents (Crowther 2005; Landon 2009; Horvath 2010; Hartling 2013; ADA 2017; Farrar 2017). This wealth of information provides a challenge for busy clinicians and women with GDM seeking evidence about optimal treatments.

1.7.1 Dietary and exercise advice for women with GDM

The first-line treatment for women with GDM is usually individualised dietary modification (Bonomo 2005; Crowther 2005; Landon 2009; Ministry of Health 2014; NICE 2015; ADA 2017). Dietary advice aims to ensure a woman's diet normalises capillary blood glucose (CBG) concentrations, provides sufficient energy and nutrients to enable normal fetal growth and minimises excessive maternal weight gain (Dornhorst 2002; Ministry of Health 2014; NICE 2015; ADA 2017). It is recommended in the literature that all women diagnosed with GDM need to have the opportunity to consult with a diabetes specialised dietitian to determine the appropriate individualised diet recommendations (Cheung 2009; NICE 2015).

Physical activity is usually recommended as low-impact activities, such as swimming, walking stationary cycling and aerobics (ACOG 2015; Padayachee 2015). Regular and sustained physical activity effects the shifting of fuel usage by muscle movement from non-esterified fatty acids (NEFAs) to a blend of NEFAs, glucose, and muscle glycogen (Sigal 2004; Asano 2014). This improves insulin sensitivity (Sigal 2004; Clapp 2006). Like dietary interventions, physical activity aims to achieve optimal glycaemic control for the woman with GDM to improve maternal and infant outcomes.

1.7.2 Lifestyle interventions for women with GDM

Lifestyle interventions are frequently referred to as a combination of physical activity and dietary interventions (Garrison 2015; Piper 2017). This is a limited definition as others in the literature refer to it as needing to include additional interventions such as psychosocial care, smoking cessation, diabetes

self-management education (DSME) and diabetes self-management support (DSMS) (Haas 2013; ADA 2017).

When optimal glycaemic control is unachievable by dietary and exercise interventions or combined with other lifestyle management for women with GDM, pharmacological hypoglycaemic agents are considered. These are usually subcutaneous insulin or oral hypoglycaemic agents (OHA's) (NICE 2015; ADA 2017; Farrar 2017).

1.7.3 Pharmacological treatments for women with GDM

Subcutaneous insulin is the recommended first-line medication for treating hyperglycaemia for women with GDM because it does not cross the placenta to a measurable extent (Mpondo 2015; ADA 2017). However, there has been an increase in the use of OHA's as an alternative to subcutaneous insulin for the treatment of women with GDM due to lower costs, ease of administration and acceptability (Ogunyemi 2011; Berggren 2013; Ryu 2014; Balsells 2015). This has been guided mainly by clinical preference and national clinical practice guidelines (Ministry of Health 2014; NICE 2015). The most commonly used OHA's are metformin (a biguanide) and glyburide (glibenclamide, a sulfonylurea). Both OHA agents cross the placenta to the fetus, with metformin likely crossing to a greater extent than glyburide (ADA 2017). Several publications have investigated the safety of using metformin and glyburide and compared to subcutaneous insulin in pregnancy for GDM and found both OHA's are not associated with short term adverse morbidity or mortality (Rowan 2008; Dhulkotia 2010; Maymone 2011; Kavitha 2013; Davoren 2014; Holt 2014; Kalra 2015). There is limited high-quality evidence for the long-term health of the children exposed *in utero* to metformin or glyburide.

1.7.4 Other supplementations for women with GDM

There is an increasing interest in the literature about the effect of nutraceutical supplementations to strengthening metabolic support or prevent metabolic disorders including GDM (LakshmanaPrabu 2012). Myo-inositol, which is an isomer of inositol, has been reported from small randomised controlled trials to reduce insulin resistance (Croze 2013). Further high-quality research of supplementations is needed to establish if any improve health outcomes and are safe for mothers and babies.

1.7.5 Cochrane systematic reviews

Published evidence from multiple Cochrane systematic reviews add to the body of evidence about treatment options from randomised controlled trials for women with GDM. These include different types of dietary advice for women with GDM (Han 2017), exercise for pregnant women with GDM (Brown 2017c), oral anti-diabetic pharmacological therapies for the treatment of women with GDM (Brown 2017a), dietary supplementation with myo-inositol in women during pregnancy for treating GDM (Brown 2016a), lifestyle interventions for treatment for women with GDM (Brown 2017b) and elective delivery in diabetic pregnant women (Boulvain 2001).

It is challenging for busy health professionals, consumer and guideline developers to summarise and interpret the available information from multiple Cochrane systematic reviews. Synthesising the evidence from Cochrane systematic reviews on treatments for women with GDM would facilitate the aggregation of available evidence. This could be addressed in generating a Cochrane Overview of reviews, providing a one-stop shop for the evidence of optimal treatment interventions for women with GDM and their effects on short and long-term maternal and infant health.

1.8 Cochrane Overview

Overviews of reviews bring together multiple systematic reviews addressing a set of related interventions, conditions, populations, or outcomes. It provides a map of the existing evidence (Becker 2011). A Cochrane overview of reviews uses explicit and systematic methods to search for, and identify, multiple Cochrane intervention reviews (and non-Cochrane systematic reviews, where applicable) on a similar topic for the purpose of extracting and analysing their results across important outcomes (Becker 2011). This includes quality assessments. Overviews of reviews have been used as an effective methodology to summarise evidence for complex interventions relating to pregnancy and childbirth. These include pain management for women in labour (Jones 2012); antenatal and intrapartum interventions for preventing cerebral palsy (Shepherd 2017) and interventions during the antenatal period for preventing stillbirth (Ota 2012). An Overview of reviews focusing on treatments for women with GDM and their effects on short- and long-term maternal and infant health would meet the current need for synthesised evidence. In summary, a Cochrane Overview addressing the research question of which treatments are effective for women with GDM would:

- Summarise effectiveness of multiple systematic reviews

- Provide a map of the existing evidence
- Summarise most effective interventions
- Be useful for clinicians, consumers, and clinical guideline developers in an area where evidence is scattered across many sources
- Highlight methodological issues regarding the appropriate conduct of systematic reviews
- Highlight the existence of other systematic reviews
- Encourage accessing individual systematic reviews for additional details
- Identifies potential research or evidence gaps

1.9 Glycaemic treatment targets for women with GDM

Glycaemic targets are essential for guiding the treatment of women with GDM to stabilise glucose metabolism and reduce the short- and long-term risks associated with GDM for the woman and her child (IADPSG 2010; Stewart 2014). Glycaemic control is usually measured by monitoring capillary blood glucose (CBG) concentrations to ensure they are maintained within a pre-defined threshold (Metzger 2008). Recommendations for the timing of CBG testing for women with GDM vary between diabetes in pregnancy health care providers. Recommendations may include testing CBG four to six times daily, testing on waking (fasting); before a meal (pre-prandial) and one- or two-hours after a meal (post-prandial) (Poomalar 2015; ADA 2017).

1.9.1 Glycaemic treatment target recommendations for GDM internationally

Worldwide recommendations for glycaemic treatment targets for women with GDM vary significantly (Table 1.2). These recommendations are based on consensus as there is currently a lack of high quality evidence (Metzger 2007; IADPSG 2010; Nankervis 2014; NICE 2015). Professional organisations are increasingly advocating lowering glycaemic targets for women with GDM with the aim of reducing morbidity for the women and their children (Hernandez 2015; ADA 2017). The need for high-quality trials comparing different glycaemic targets assessing short- and long-term outcomes for the women and their children is recognised (NICE 2015; Ministry of Health 2014).

Table 1.2: Treatment targets for glycaemic control from Clinical Practice Guidelines

	Fasting plasma glucose (mmol/L)	1-hour postprandial (mmol/L)	2-hour postprandial (mmol/L)
Australasian Diabetes in Pregnancy Society (Nankervis 2013; 2014) and Ministry of Health New Zealand (2014)	≤ 5.0	≤ 7.4	≤ 6.7
Canadian Diabetes Association (CDA 2013)	< 5.3	< 7.8	< 6.7
National Institute of Health and Clinical Excellence (NICE 2015)	5.3	< 7.8	< 6.4
American Diabetes Association (ADA 2013)	≤ 5.3	≤ 7.8	≤ 6.7
5th International Workshop on GDM (Metzger 2007)	5.0 to 5.5	< 7.8	< 6.7 to 7.1
Scottish Intercollegiate Guidelines Network (SIGN 2014)	4.0 to 6.0	< 8.0	< 7.0
German Diabetes Association (DDA) (Kleinwechter 2014)	3.6 to 5.3	< 7.8	< 6.7

Source: as adapted from Martis 2016a

1.9.2 Glycaemic treatment target recommendations for GDM in New Zealand

The lack of high-quality evidence for glycaemic targets in pregnant women with GDM was highlighted in the Ministry of Health (2014) guideline publication of 'Screening, Diagnosis and Management of Gestational Diabetes in New Zealand: A Clinical Practice Guideline'. The multidisciplinary guideline panel recommended the use of the following glycaemic treatment targets for women with GDM: fasting plasma glucose ≤5.0 mmol/L; 1-hour postprandial ≤7.4 mmol/L and 2-hour postprandial ≤6.7 mmol/L (Ministry of Health 2014). This recommendation was reached by consensus, identified in the guideline as a good practice point (GPP) as there was no high-quality evidence available from randomised controlled trials to make an evidence-based recommendation. The guideline included a research recommendation for a randomised control trial comparing less tight with tighter glycaemic targets in women with GDM for maternal and infant well-being (Ministry of Health 2014), as also proposed the following year in the NICE guideline (NICE 2015). Given the reported lack of high-quality evidence in

the literature, a systematic review critically analysing the evidence from randomised controlled trials may clarify the effectiveness of different glycaemic targets for women with GDM. This will provide clearer evidence to inform clinical practice addressing the research question of which glycaemic treatment targets best benefit the health of women diagnosed with GDM and their babies.

1.10 Consumer involvement

The New Zealand's Health and Disability Commissioner has identified that consumer involvement is a priority in health decision making (Coney 2004). Rationales for consumer participation apart from the relevant legislation, include empowerment of consumers to make informed choices, increasing accountability for the consumer and health professionals, increased treatment understanding and adherence by the consumer, more relevant service provision for the consumer resulting in improved quality of health care (Coney 2004; Kelson 2005; NICE 2013; Hack 2017).

Legislations such as the Health and Disability Commissioner Act (1994) and the Health and Disability Services Consumers' Rights Regulation (1996) support this. The Cochrane Collaboration, an international organisation, concurs (Morley 2016). It is therefore recommended that in any research involving health consumers, their experiences are investigated to support the research results. Definitions of 'consumers' vary in the literature but most often is defined as 'a user of health care' (Coney 2004; Kelson 2012). This can mean: an individual patient, caregivers, the patients' family and friends, members of the public, community organisations, advocates representing the interests of patients, and are distinct from health professionals and providers of health services (Coney 2004; Kelson 2012).

In 2015 the National Institute for Health and Care Excellence (NICE) published their up-dated guideline for Diabetes in pregnancy: management from preconception to the postnatal period and recommends further robust qualitative studies are needed to explore barriers and enablers for women with GDM to maintain optimal glycaemic control (NICE 2015).

The New Zealand TARGET Trial, is a randomised control trial, that is investigating different glycaemic targets for maternal and infant well-being. Following the NICE (2015) research recommendation for explorations of barriers and enabler for women with GDM in maintaining optimal glycaemic control, this provided the opportunity to conduct a survey and interview with women diagnosed with GDM.

1.10.1 The New Zealand TARGET Trial

Based on the Ministry of Health (2014) and NICE (2015) research recommendations, and in an attempt to provide better quality evidence, the TARGET Trial (Optimal glycaemic targets for gestational diabetes: a step-wedged randomised trial) is being conducted to assess if tighter glycaemic targets compared with less tight glycaemic targets for women with GDM will reduce perinatal morbidity without adverse health consequences (Australian New Zealand Trials Registry – ACTRN 12615000282583; New Zealand Health and Disability Ethics committee (HDEC) Ref. 14/NTA/163 and research registration number 1965).

The glycaemic targets compared in the TARGET Trial are:

- for the less tight glycaemic targets: fasting plasma glucose <5.5 mmol/L; 1-hour postprandial <8.0 mmol/L; 2-hour postprandial <7.0 mmol/L (as recommended for current glycaemic treatment targets by the American Diabetes Association (ADA 2013) and
- for the tighter glycaemic targets of fasting plasma glucose ≤5.0 mmol/L; 1-hour postprandial ≤7.4mmol/L; 2-hour postprandial ≤ 6.7mmol/L (as recommended by the New Zealand Ministry of Health (Ministry of Health 2014).

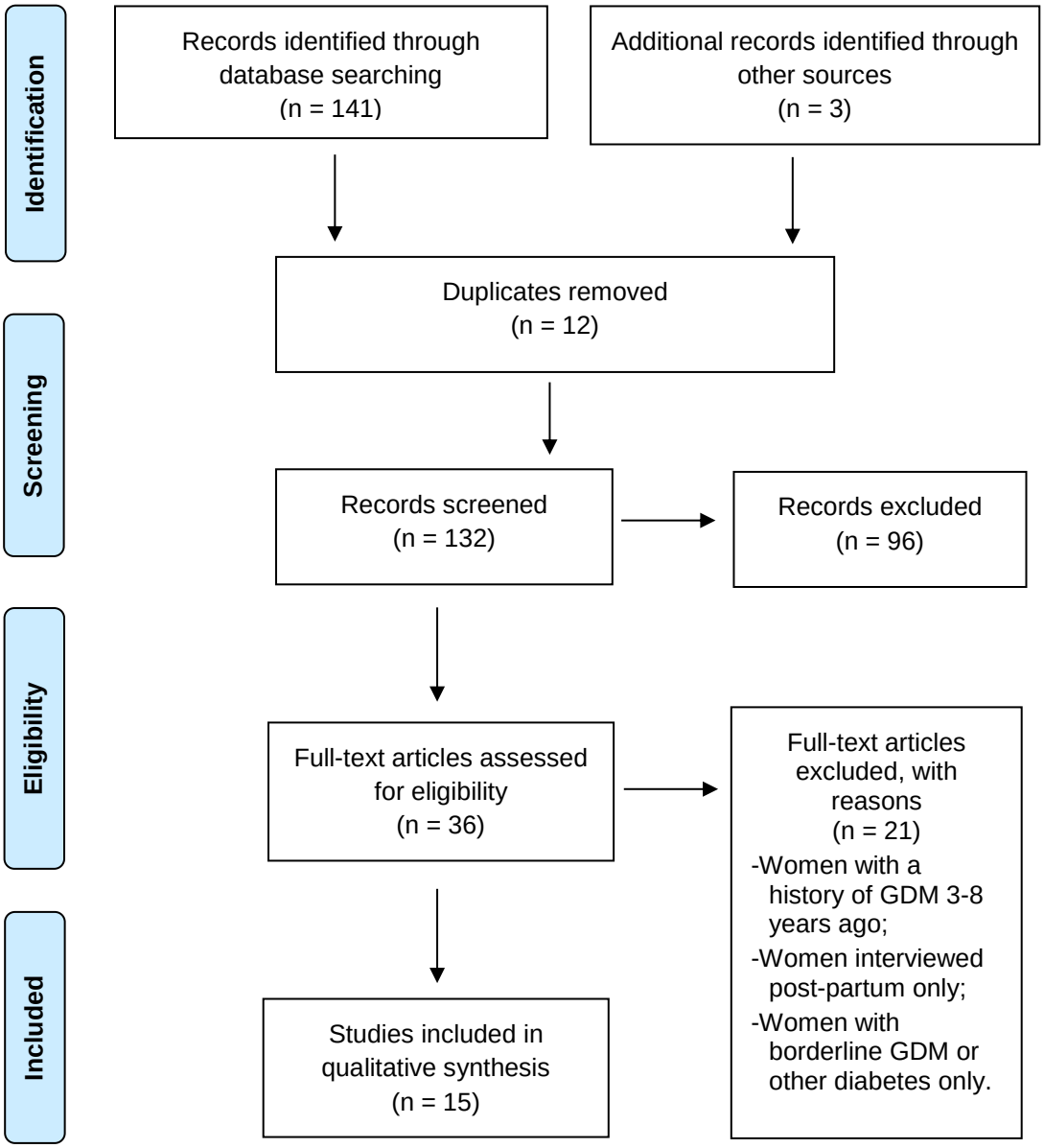
The TARGET Trial through its randomised stepped wedge research approach will implement tighter glycaemic targets for women with GDM in New Zealand. It is important to explore what hinders or enables women with GDM in achieving these tighter glycaemic targets. Diabetes in Pregnancy services and health professionals would be able to consider how best to support women to self-manage in achieving optimal glycaemic control. Self-management is an important aspect for optimal glycaemic control as the woman learns to test her capillary blood glucose and adjust her lifestyle to stay within the recommended glycaemic targets. This has not been investigated in New Zealand.

1.10.2 Women's views and experiences, barriers, and enablers, with glycaemic treatment target for current GDM - in the literature

An in-depth literature search of four relevant databases (MEDLINE (Ovid)/Pubmed, Embase, CINAHL, Google Scholar) for peer reviewed articles published between 1980 and 2017 using the search terms: gestational diabetes mellitus, women's' views, self-management, capillary blood glucose control, glycaemic control, enablers and barriers with a number of different word combinations and truncations was conducted and up-dated 30th October 2017 (Figure 1.2). A total of 15 published primary studies

were considered relevant (Table 1.3) and three systematic reviews. Three studies were conducted in Australia, two studies each in Canada, United Kingdom (UK) and USA and one study each in Austria, Brazil, Italy, Sweden, Thailand, and Vietnam. No New Zealand studies were identified within this search. Two of the 15 primary studies reported the recommended glycaemic targets for the participating women with GDM (Table 1.3). One Australian study (Carolan 2012b; Carolan 2013) published two articles with results from the same cohort of 15 pregnant women with GDM and was counted as one publication (Table 1.3).

Figure 1.2: Literature search - PRISMA flow diagram



Source: as adapted from Moher 2009

Table 1.3: Included publications of primary studies from literature search

Author Title of Study	Design/Method	Setting	Participants	Results/Findings	Glycaemic Targets
1. Jirojwong 2017 Going up, going down: the experience, control, and management of gestational diabetes mellitus among Southeast Asian migrant women living in urban Australia	Qualitative, face-to-face interviews with bilingual research assistants	Antenatal clinics at two metropolitan hospitals in Sydney, NSW, Australia	19 women diagnosed with GDM who were born in Vietnam, Cambodia, Thailand, or Lao People's Democratic Republic (Laos)	A diagnosis of GDM conferred an unanticipated 'up and down' experience for this group of Southeast Asian women.	Not reported
2. Youngwanichsetha 2017 Lived experience of blood glucose self-monitoring among pregnant women with gestational diabetes mellitus: a phenomenological research	Qualitative, semi- structured interviews	Antenatal care units, diabetes clinics and obstetric wards at two government hospitals in southern Thailand which are the referral centres providing management of pregnancy complicated with GDM	30 Thai women with GDM practising capillary blood glucose self-monitoring, diagnosed between 24-30 weeks gestation	Three themes: 1. Being worried about diabetes and blood testing 2. Trying to control it 3. Being patient for the child	Post prandial 5.0 - 6.6 mmol/l
3. Yee 2016 Which factors promote diabetes self-care among low-income, minority pregnant women?	Qualitative, in-depth semi-structured interviews	Chicago, USA, urban academic medicaid-funded perinatology clinic, low-income community	10 English-speaking pregnant women ages 18 and over, with GDM or Type 2 diabetes mellitus (T2DM) (5 women with GDM and 5 women with T2DM) 30 weeks gestation.	1. Diabetes self-efficacy and knowledge 2. External motivation 3. Supportive environment 4. Self-regulation	Not identified
4. De Silvia Sousa 2016 Does information retention after attending a multidisciplinary group with health professionals increase adherence to treatment for women with GDM?	Quantitative, phone survey	São Paulo, Brazil (no further information)	122 women with GDM	119/122 (97.5%) women were managing to do self-glucose monitoring 21/122 (17.2%) women reported having difficulty with finger pricking 24/122 (19.7%) women found it too difficult to follow the diet 23/122 (18.9%) women unable to reach meal frequency 47/122 (38.5%) women reported having ingested sugar in the days following the guidance in multidisciplinary group. Conclusion suggests closer long-term follow-up and clearer information given.	Not identified

Author Title of Study	Design/Method	Setting	Participants	Results/Findings	Glycaemic Targets
5. Draffin 2016 Exploring the needs, concerns and knowledge of women diagnosed with gestational diabetes: A qualitative study	Qualitative, five focus groups	At outpatient diabetes care clinics at three National Health Service (NHS) hospitals in the United Kingdom (Ireland)	19 women, multi-ethnic, either with current GDM diagnosis or postnatal with recent history of GDM	1. Women experienced a steep learning curve when initially diagnosed and eventually became skilled at managing their disease effectively. 2. The use of insulin was associated with fear and guilt. 3. Diet advice was sometimes complex and not culturally appropriate. 4. Women appeared not to be fully aware of short or long-term consequences of GDM.	Not reported
6. Hirst 2015 Does a smartphone-based, interactive blood glucose management system for women with GDM increase glucose monitoring satisfaction?	Quantitative, structured questionnaire, the Oxford Maternity Diabetes Treatment Satisfaction Questionnaire (OMDTSQ) with free text at the end	Oxford University Hospitals NHS Trust, Oxford, United Kingdom (England)	52 women with GDM, English speaking, not requiring pharmacological therapy, after one week of CBG monitoring, diagnosed prior to 34 weeks gestation	1. Intervention promoted women's satisfaction with care. 2. Encouraging results need confirmation in a larger clinical study.	Not reported
7. Kaptein 2015 The subjective impact of a GDM among ethnically diverse pregnant women: A qualitative study	Qualitative, semi structured telephone interviews	Women's College Hospital, Toronto, Canada	19 women with GDM of diverse backgrounds	1. Heightened pressure to fulfil multiple roles, financial impact, and a disconnect between diabetes-prevention recommendations and their cultural practices. 2. GDM diagnosis positive effects: to make health behaviour changes after a GDM diagnosis viewing it as a wake-up call to modify lifestyles.	Not reported
8. Hui 2014 Barriers and coping strategies of women with gestational diabetes to follow dietary advice	Qualitative, Food Choice Map (FCM); semi-structured interview and demographic questionnaire	Department of Internal Medicine, University of Manitoba, Winnipeg, Canada	30 women with GDM from the Winnipeg area	Barriers: 1. Personal food preference conflicted with dietary advice; 2. Eating in different social environments where food choice and portions were out of control and food choice decisions were affected by social norms	Not reported

Author Title of Study	Design/Method	Setting	Participants	Results/Findings	Glycaemic Targets
				3. Lack of knowledge and skills in dietary management and lack of a tailored dietary plan.	
9. Carolan 2013 Women's experiences of gestational diabetes self-management: A qualitative study	Qualitative, semi-structured interviews and one focus group	Sunshine Hospital, Melbourne, Australia	15 women diagnosed with GDM between 28-38 weeks gestation	Themes identified: 1. The shock of diagnosis; 2. Coming to terms with GDM 3. Working it out/learning strategies 4. Looking to the future. 5. Having a supportive environment	Not reported
9. Carolan 2012b Women's experiences of factors that facilitate or inhibit gestational diabetes self-management	Qualitative, semi structured interviews and one focus group	Sunshine Hospital, Melbourne, Australia	15 women diagnosed with GDM between 28-38 weeks gestation	Barriers included: 1. Time pressures; 2. Physical constraints; 3. Social constraints; 4. Limited comprehension of requirements; 5. Insulin seen as an easier option. Enablers included: 1. Thinking about the baby; 2. Psychological support from partners and families.	Not reported
10. Hirst 2012 Women with gestational diabetes in Vietnam: a qualitative study to determine attitudes and health behaviours	Qualitative, four focus groups	Hung Vuong Hospital, Ho Chi Minh City, Vietnam	34 women with GDM diagnosed between 28-38 weeks gestation	1. Women felt confusion, anxiety, and guilt about GDM 2. Many perceived their baby to be at increased risk of death 3. Advice to reduce dietary starch was confusing 4. Being hungry or starving most of the time 5. Unaware of appropriate food substitutions 5. Concerned about transmission of GDM through breast milk. 6. Small group sessions and information leaflets could benefit 7. There is a need for culturally appropriate clinical education and health promotion activities for women with GDM in Vietnam.	Not reported

Author Title of Study	Design/Method	Setting	Participants	Results/Findings	Glycaemic Targets
11. Lapolla 2012 Quality of life, wishes, and needs in women with gestational diabetes: Italian DAWN Pregnancy Study	Quantitative, questionnaire. Comparison between Italian and immigrant women with GDM	10 Italian centres specialised in the care of pregnant women with diabetes including GDM. Department of Medicine, University of Padova, Italy	198 Italian women and 88 Immigrant women (with 27 different nationalities) with GDM diagnosed between 25-29 weeks gestation	In both groups: 1. GDM caused anxiety 2. One-third of women feared their child could contract diabetes at delivery and/or have congenital malformations 3. Some women had trouble in following treatment regimens: the major concern being dietary advice and blood glucose testing. 4. Most women were satisfied (34%) or highly satisfied (60%) 5. The degree of co-operation between diabetes specialists and gynaecologists was considered unsatisfactory. 5. To optimise maternal and fetal outcomes, educational projects, and improved communication between women with GDM and the healthcare provider team are recommended. 6. Only difference was the women who had immigrated had better family support	FPG < 5.3 mM and 2-hour post-prandial plasma glucose < 6.7 mM
12. Trutnovsky 2012 Gestational diabetes: women's concerns, mood state, quality of life and treatment satisfaction	Qualitative and quantitative, semi-structured interview and three questionnaires	University of Graz GDM specialist clinic, Graz, Austria	27 diet-treated and 18 insulin-treated women with GDM	1. Most dominant concern identified as the baby's health and was the main motivational treatment factor. 2. Treatment satisfaction was generally high and further Increased over time 3. Quality of life and mood state significantly dropped over time. 4. Low awareness of personal long-term implications 5. Specific postpartum information seems necessary to ensure prompt recognition and treatment of any recurrence of diabetes.	Not reported

Author Title of Study	Design/Method	Setting	Participants	Results/Findings	Glycaemic Targets
13. Bandyopadhyay 2011a Lived experience of gestational diabetes mellitus among immigrant South Asian women in Australia	Qualitative, face-to-face in-depth interviews	The Royal Women's Hospital, Parkville, Victoria, Australia	17 immigrant women from South Asia recently diagnosed with GDM living in Australia, able to speak Hindi, Bengali or English	1. Women and their partners were upset by the diagnosis. 2. Importance of cultural appropriate dietary advice 3. Effective support for fluctuating glucose levels, as these raised significant concerns for the women fearing the commencement of insulin injections. 4. Different attitudes to exercise in pregnancy 5. Diabetes in Pregnancy services should consider the use of bilingual diabetes advocates and the appropriate use of interpreters.	Not identified
14. Persson 2010 From stun to gradual balance – women's experiences of living with gestational diabetes mellitus	Qualitative, semi-structured interviews	32 local health care centres, Umea, North Sweden	10 women with current GDM diagnosed around 28 weeks gestation	1. From 'stun to gradual balance' emerged as the core category. 2. Being diagnosed with GDM was not only perceived as a medical complication threatening the pregnancy 3. Also seen as an indicator of a future Type 2 diabetes mellitus	Not reported
15. Spirito 1992 Does diabetes knowledge increase regimen compliance and metabolic control during pregnancy for women with GDM and pre-existing diabetes?	Qualitative and quantitative, interviews and completion of an adapted version of the Diabetes Compliance Questionnaire and Diabetes in Pregnancy Knowledge Screen	Rhode Island Hospital, USA.	72 women English speaking (27 women with pre-existing insulin-dependent and noninsulin-dependent diabetes mellitus and 45 women with GDM), between 28 and 40 weeks gestation.	1. Efforts to increase knowledge of diabetes in pregnant women may result in compliance improvement in selected aspects of the diabetic regimen. 2. Age and socioeconomic status, knowledge appears to affect regimen compliance.	Not reported

Three publications reported results from surveys (Table 1.3). One UK based survey explored, with 52 women with GDM, if a smart-phone based interactive glucose management system would increase satisfaction with glucose monitoring (Hirst 2015). Findings appear to increase women's satisfaction with care and a recommendation for a larger clinical study is posed. The second survey based in Brazil investigated if information retention after attending a multidisciplinary group with health professionals increased adherence to treatment for women with GDM (De Silvia Sousa 2016). One hundred and twenty-two women with GDM were surveyed and findings suggest that the women with GDM in their study needed closer long-term follow up and had a need for clearer information. The third survey reported findings from 199 Italian women with GDM and 88 immigrant women with GDM (27 different nationalities) and compared if there were any different experiences between the two groups (Lapolla 2012). The findings suggested the only difference was that the women who had immigrated identified better family support. The conclusions were for optimising maternal and fetal outcomes, for both groups, there is a need for improved communication between women with GDM and between the healthcare providers.

Seven qualitative studies used either semi-structured interviews or focus groups to elicit experiences from pregnant women living with GDM and used thematic analysis to analyse their findings (Persson 2010; Bandyopadhyay 2011a; Hirst 2012**;** Carolan 2013; Kaptein 2015; Draffin 2016; Jirojwong 2017) (Table 1.3). Themes identified were similar among these studies in that women diagnosed with GDM were initially shocked, moved through to acceptance of their diagnosis as time passed, were motivated by their babies and that a supportive environment made a difference. Glycaemic treatment targets for the women in the included studies were not reported.

Three qualitative studies specifically investigated enablers and barriers for women with GDM through either face-to-face or phone semi-structured interviews (Carolan 2012b; Hui 2014; Yee 2016) (Table 1.3). Hui (2014) investigated enablers and barriers for 30 Canadian women with GDM to follow dietary advice. Thematic analysis identified a lack of an individualised dietary plan and difficulty following dietary advice when food preference conflicted with dietary advice at home and in different social settings.

A USA study of 10 minority, low-income pregnant women with diabetes (five women with GDM and five women with T2DM) investigated what factors promoted diabetes self-care and found long-term goal setting, supportive environment, external motivation, and knowledge as enabling (Yee 2016).

A qualitative study with 15 Australian women with GDM identified barriers as time, physical and social constraints, limited understanding of requirements and seeing insulin as an easier option. Enablers facilitating self-management included being motivated by the baby and psychological support from partners and family (Carolan 2012b).

A further two-mixed method studies (interviews and questionnaires) were identified through the search (Table 1.3). One study based at Rhode Island, USA, investigated specifically if diabetes knowledge increased treatment compliance with 72 women with diabetes (45 women with GDM and 27 women with pre-existing diabetes) (Spirito 1992). The combined results from two questionnaires and interviews found that efforts to increase knowledge of diabetes may result in improved compliance for selected aspects of the diabetic regimen (undefined). The authors found that age, socioeconomic status and knowledge specific to the diabetic treatment during pregnancy, appeared to affect regimen compliance. This is a relatively old study and with the event of the information explosion via the internet this may result in different findings if the study would be repeated.

The second mixed-method study from Austria was interested in the mood state and quality of life for women with GDM and included 27 diet-treated and 18 insulin-treated women with GDM (Trutnovsky 2012). The authors found similar findings to the thematic analysis in the qualitative studies above that the baby motivates treatment factors. Additionally, they found for both groups the quality of life and mood state significantly dropped over time and the existence of low awareness for personal long-term health implications. Recommendations included for health professionals to increase their assessment of mental well-being for women with GDM and ensure clear information for long-term risks is provided.

Only one qualitative study from Thailand, focused on the lived experience of CBG monitoring among 30 pregnant women diagnosed with GDM (Youngwanichsetha 2017) (Table 1.3). Through semi-structured face-to-face interviews emerging themes included being worried about diabetes and blood testing, trying to control it and being patient for the child. Only postprandial targets (timing not identified) were stated as needing to be between 5.0 - 6.6 mmol/l for all women involved in the study.

The search identified three systematic literature reviews. One review identified 42 qualitative and quantitative studies with data from 7949 women in number of countries with the aim to identify enablers and barriers for women who had experienced GDM to postpartum healthcare seeking (Van Ryswyk 2015). While this literature review did not include pregnant women with current GDM, which is of interest

for this thesis, it is relevant to note that one of the findings identified that women still remembered that the diagnosis of GDM was a concerning or upsetting experience. This appears to be a recurring theme in the literature. The authors concluded that provision of improved GDM education, as well as positive and pro-active care from diagnosis until postpartum follow-up may increase healthcare seeking by women with recent GDM.

Another literature review, which included 15 qualitative and four quantitative studies, exploring the beliefs, values, perceptions, and experiences of women with a diagnosis or history of GDM found that women's initial reaction to being diagnosed with GDM generated negative feelings, which overtime led to accepting and adapting of the condition (Devsam 2013). The review did not report on how many women or studies were prospective or retrospective nor made an attempt to compare if healthcare seeking beliefs for future T2DM made a difference according when women were interviewed. It did propose a framework for clinical assessments and care of women diagnosed with GDM that may be used by midwives.

Women's perceptions of future diabetes risk and views on diabetes prevention was explored by Parsons 2014. The review reported on 16 qualitative studies with 302 women apparently diagnosed with GDM. It became evident to the thesis author through reading the review that some of the studies included women who had a history of GDM. Some of the included studies reported the experiences for women diagnosed with GDM and the findings recommend addressing the emotional impact of GDM as this would improve diabetes prevention behaviour and offering an intervention that fits with women's multiple roles as caregivers, workers, and patients, and focuses on the health of the whole family.

There is limited evidence of qualitative and quantitative explorations of women's views, experiences, barriers, and enablers with current GDM relating specifically to their ability to stay within their recommended glycaemic treatment targets. There have been no studies published in New Zealand to date. Maternity care varies greatly from country to country. For example, maternity care in the USA is provided to a large extent by obstetricians being the lead professional including uncomplicated pregnancies and births. In contrast to New Zealand, midwives are the lead carer for women with uncomplicated pregnancies and often provide shared-care for women with GDM (NZCOM n.d.; Ministry of Health 2012). There is a need to investigate pregnant women's views and experiences, barriers, and enablers with current GDM including a comparison about their glycaemic treatment targets for the New Zealand context.

1.11 Implementation science/knowledge translation

Implementation science or knowledge translation, as it is increasingly known (Grimshaw 2012; Strauss 2013; Khalil 2016), refers to the study of methods to promote the integration and uptake of research findings and evidence through optimal approaches into clinical practice and health care policy (WHO 2014; NIH 2016). The overarching goal is to create generalisable knowledge that can be contextualised and applied across settings to achieve sustained health improvements and reduce the evidence gap (Madon 2007; Burke 2012; Wensing 2013). Key stakeholders in knowledge translation include not only health professionals, researchers, policy makers but also consumers, as this can ensure that the information is understandable from the consumer perspective and relevant to their context (Tugwell 2007; Pearson 2012; Légaré 2014). Implementation science or knowledge translation has an important role in identifying enablers and barriers for effective health programming, policy making and evidenced-based treatment implementations (Grimshaw 2012; Légaré 2014; WHO 2014). For women with GDM enabler and barrier identification may support and enable effective behaviour change in achieving optimal glycaemic control.

1.11.1 Barriers and enablers identification

Implementation science or knowledge translation has contributed to the growing interest in the literature to the identification of enablers and barriers to guide effective implementation of practice and behaviour change (Grol 2003; NICS 2006; Michie 2011; Cane 2012; Nielsen 2012). Translating knowledge into practice needs to be tailored to specific enablers and barriers in order for clinical practice to change or adherence to treatment to be achieved (Wensing 2010; Straus 2013; Baker 2015). Only “14% of significant research findings ever enter the real-word context” (p. 178) and this is believed to be due to the lack of clear understanding of how to implement the research results without local contextual enabler and barrier identification (Gitlin 2013). This highlights the importance that knowledge translation requires to be evidence-informed through contextual and meaningful enablers and barriers underpinned by a theoretical approach with a clear validated framework (Baker 2015; Nilsen 2015).

1.11.2 Theoretical Domains Framework for barrier and enabler identification for women with GDM

The use of the Theoretical Domains Framework (TDF) has been identified in the literature as an effective tool to identify enablers and barriers and to understand, inform and facilitate effective behavioural

change and health service provision (Michie 2005; Michie 2008; Michie 2011). It resulted from an increasing belief that applying psychological explanations for behaviour change, based on health and social psychology theories, may explain health-related behaviour change more effectively and result in a more targeted and informed implementation strategy, rather than applying single models to predict behaviour (Michie 2005; Davies 2010; Atkins 2017). The TDF was developed using an expert consensus process and validation to identify psychological and organisational theory relevant to behaviour change (Michie 2005; Michie 2008; Michie 2011; Cane 2012). The most recent validated version of the TDF includes 14 domains and their component constructs (Cane 2012, Atkins 2017) (Table 1.3). The TDF has been used in health care to identify factors influencing health practitioner's clinical behaviour and behaviour change (Davies 2010; Cane 2012; French 2012) but is increasingly used to identify enablers and barriers for the consumer in order to understand their experiences and views to adherence of treatment and lifestyle changes (Burgess 2014; Nicholson 2014; Penn 2014; McGoldrick 2016).

Table 1.4: Refined Theoretical Domains Framework and its constructs

Theoretical Domains	Generic Definitions	Constructs
Knowledge	An awareness of the existence of something	- Knowledge (including knowledge of condition/scientific rationale) - Procedural knowledge - Knowledge of task environment
Skills	An ability or proficiency acquired through practice	- Skills - Skills development - Competence - Ability - Interpersonal skills - Practice - Skill assessment
Social/Professional Role & Identity	A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting	- Professional identity - Professional role - Social identity - Identity - Professional boundaries - Professional confidence - Group identity - Leadership - Organisational commitment
Beliefs about capabilities	Acceptance of the truth, reality or validity about an ability, talent, or facility that a person can put to constructive use	- Self-confidence - Perceived competence - Self-efficacy - Perceived behavioural control - Beliefs - Self-esteem - Empowerment - Professional confidence
Optimism	The confidence that things will happen for the best or that desired goals will be attained	- Optimism - Pessimism - Unrealistic optimism - Identity

Theoretical Domains	Generic Definitions	Constructs
Beliefs about consequences	Acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation	- Beliefs - Outcome expectancies - Characteristics of outcome expectancies - Anticipated regret - Consequents
Reinforcement	Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus	- Rewards (proximal/distal, valued/not valued, probable/improbable) - Incentives - Punishment - Consequents - Reinforcement - Contingencies - Sanctions
Intentions	A conscious decision to perform a behavior or a resolve to act in a certain way	- Stability of intentions - Stages of change model - Transtheoretical model and stages of change
Goals	Mental representations of outcomes or end states that an individual wants to achieve	- Goals (distal/proximal) - Goal priority - Goal/target setting - Goals (autonomous/controlled) - Action planning - Implementation intention
Memory, attention, and decision processes	The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives	- Memory - Attention - Attention control - Decision making - Cognitive overload/tiredness
Environmental context and resources	Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behaviour	- Environmental stressors - Resources/material resources - Organisational culture/climate - Salient events/critical incidents - Person × environment interaction - Barriers and facilitators
Social influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings or behaviours	- Social pressure - Social norms - Group conformity - Social comparisons - Group norms - Social support - Power - Intergroup conflict - Alienation - Group identity - Modelling
Emotion	A complex reaction pattern, involving experiential, behavioural and physiological elements, by which the individual attempts to deal with a personally significant matter or event	- Fear - Anxiety - Affect - Stress - Depression - Positive/negative affect - Burn-out
Behavioural regulation	Anything aimed at managing or changing objectively observed or measured actions	- Self-monitoring - Breaking habit - Action planning

Source: as adapted from Cane 2012; Atkins 2017

1.12 Conclusion

Short- and long-term health implications for the woman diagnosed with GDM and her baby have been consistently reported. The prevalence of GDM is increasing globally and in New Zealand. Evidence-based practice requires accurate knowledge translation of treatments to affect the reduction of the health risks for women with GDM and their children. The impact of the evidence for effective treatments and optimal glycaemic control for women with GDM appears to be limited due to the difficulty of accessibility to the evidence as it is either published in multiple systematic reviews for treatments for women with GDM, in several randomised controlled trials for glycaemic treatment targets for women with GDM or no publications available for New Zealand women's view, experience, enablers and barriers to achieving optimal glycaemic control.

Therefore, this thesis has the following key aims:

1.13 Thesis aims and research questions

1. **To synthesise the current research evidence of Cochrane systematic reviews on treatments for women with GDM and to identify specific research gaps of treatments for women with GDM requiring further primary research.**

   To achieve this aim, I will conduct a Cochrane Overview of reviews to summarise effective treatment options for women with GDM from published Cochrane systematic reviews. The Overview will be used to highlight where there are current knowledge gaps in the evidence and focuses on the research question:

   - Which treatments are effective for women with GDM?

2. **To synthesise and assess the current research evidence from randomised controlled trials on the effect of different glycaemic targets for women with GDM and their children and to identify specific research gaps of glycaemic targets to guide treatment for women with GDM requiring further primary research.**

   To achieve this aim, I will conduct a Cochrane systematic review that synthesises the current evidence from randomised controlled trials of different treatment targets for glycaemic control and their effective outcomes for women with GDM and their babies, including the identifying any gaps of knowledge in the evidence and focuses on the research question of:

- Which glycaemic treatment targets best benefit the health of women diagnosed with GDM and their babies?

3. **To investigate how women with GDM view their glycaemic treatment targets and identify the barriers and enablers for them in achieving optimal glycaemic control.**

   To achieve this aim, I will conduct a face-to-face survey to investigate barriers and enablers focusing on the research question:

   - What do women with GDM say are the barriers and enablers for their glycaemic targets, from a quantitative research perspective?

4. **To examine behavioural factors impacting on women with GDM in achieving optimal glycaemic control.**

   To achieve this aim, I will conduct semi-structured interviews with women with GDM investigating their experiences, barriers, and enablers in achieving their recommended glycaemic treatment targets, from a qualitative perspective, using the TDF framework for analysis focusing on research questions:

   - What are women's experiences, barriers, and enablers with their glycaemic targets?
   - What is it like for a woman with GDM to monitor her capillary blood glucose (CBG) concentration?
   - What affects a woman's CBG concentrations and how does she maintain optimal CBG control with this knowledge?
   - What support have women found helpful/not helpful in learning about and maintaining optimal CBG control?

Chapter 2: Synthesising the evidence from Cochrane systematic reviews on treatments for women with gestational diabetes mellitus

2.1 Preface

This chapter presents an Overview of Cochrane systematic reviews published in the Cochrane Database of Systematic Reviews entitled '**Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews'.** The chapter includes the completed Cochrane Overview, prepared following production of the overview protocol that was peer reviewed and published in the Cochrane Library (Martis 2016b). This Overview summarises the available evidence from existing Cochrane systematic reviews on the effectiveness of treatments for women with GDM and their infants. It includes quality assessments for the included studies and the pre-specified primary and secondary outcomes.

The chapter aims to address Research Question 1: Which treatments are effective for women with GDM?

The chapter contains the unaltered manuscript submitted for publication. The abstract and key words were removed as directed by the University of Auckland (2016) *Guide to thesis and dissertations*. The 'Plain Language Summary' from the submitted manuscript is presented at the end of the chapter.

2.2 Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews

2.2.1 Background

Gestational diabetes mellitus (GDM) is a condition that may occur in the second half of pregnancy when blood glucose control is more difficult to achieve, leading to hyperglycaemia (abnormally high concentration of glucose in the blood) that may affect the woman and her baby (ADA 2004; Holt 2014). The World Health Organization (WHO 2013) defines GDM as "Carbohydrate intolerance resulting in hyperglycaemia or any degree of glucose intolerance with onset or first recognition during pregnancy usually from 24 weeks gestation onwards" and resolves following the birth of the baby. This definition clearly excludes women who may have undiagnosed pre-existing type 1 (T1DM) or type 2 diabetes (T2DM) first detected during screening in pregnancy (Nankervis 2013).

Recognised risk factors for developing GDM include obesity, advanced maternal age, weight gain in pregnancy, family history of diabetes and previous history of GDM, macrosomia (large baby), or unexplained stillbirth (Mokdad 2003; Yogev 2004; Boney 2005; Rosenberg 2005; Zhang 2010; Teh 2011). Certain ethnicities, such as Asian, African American, Native American, Hispanic, and Pacific Island women have an increased risk (Rosenberg 2005; Schneider 2012).

The prevalence of GDM is increasing globally and has been documented with significant variation between 2% to 26% depending on the ethnicity of the population screened and the diagnostic criteria used (Cheung 2003; Ferrara 2007; Sacks 2012; Nankervis 2013; Ministry of Health 2014; NICE 2015). The reported global obesity epidemic is likely to increase the incidence of GDM (Zhang 2010; Schneider 2012) and a recurrent GDM diagnosis in subsequent pregnancies for women who have had previously been diagnosed with GDM (Bottalico 2007; England 2015; Poomalar 2015). Therefore, GDM is a serious public health issue.

Successful glycaemic treatments for GDM have the potential to significantly impact on the short- and long-term health for the woman and her baby. Treatments for GDM aim to keep glucose levels within the recommended glycaemic reference range to prevent maternal hyper- or hypoglycaemia. Treatments may include dietary and exercise advice, subcutaneous insulin, oral hypoglycaemic agents, such as pharmacological medications, dietary supplements or nutraceuticals, antenatal breast milk expression,

induction of labour or caesarean section (Horvath 2010; Kavitha 2013; Bas-Lando 2014; Forster 2014; Ryu 2014; Kalra 2015).

Currently there are several Cochrane systematic reviews assessing different treatment for women with GDM. This makes it difficult for clinicians, consumers, and guideline developers to easily interpret the available information. A Cochrane overview of systematic reviews would provide summary evidence of the effectiveness for each treatment for women with GDM and the effects on relevant health outcomes as a one-stop resource for health professionals, consumers, and guideline developers to simplify clinical treatment decision-making, and assist with the process of guideline development.

Description of the condition

During pregnancy the continuous supply of appropriate and balanced nutrients from the pregnant woman to her baby is essential for optimal health and growth. Glucose is the primary source of energy for the fetus (Wilcox 2005; Hay 2006). Insulin is a peptide hormone secreted by the β cells of the pancreatic islets of Langerhans and maintains normal glucose concentration by facilitating cellular glucose uptake, regulating carbohydrate, lipid, and protein metabolism, and promoting cell division and growth (Wilcox 2005). Either inadequate insulin secretion (such as in T1DM) or insulin resistance (such as in T2DM or GDM) (Devlieger 2008; Petry 2010) can result in hyperglycaemia. During the second half of pregnancy, insulin sensitivity falls by about 50% (Di Cianni 2003; Lain 2007). This is a normal physiologic response ensuring that the growing fetus receives sufficient glucose and other nutrients from the mother via the placenta (Buchanan 1991). In some pregnant women abnormal insulin resistance may occur if they are unable to compensate for the increased demand of insulin (Ragnarsdottir 2010; McCance 2011; Catalano 2014). This results in GDM (ADA 2004; Holt 2014). It is known that the maternal-fetal placental glucose transfer favours the fetus (Suman Rao 2013; Sadovsky 2015). Women with GDM therefore transfer higher amounts of glucose to the fetus when uncontrolled severe and prolonged maternal hyperglycaemia is present (Wilcox 2005), resulting in a baby born large-for-gestational age (Ornoy 2005; Metzger 2008; Young 2013).

Lapolla 2005 suggests the two main contributors to insulin resistance include increased maternal adiposity and the insulin desensitising effects of hormones produced in the pregnancy, especially in the placenta. As the placenta grows during the pregnancy, so does the production of the placental hormones, leading to an insulin-resistant state (Evans 2009). GDM usually resolves promptly following the birth of the baby and the placenta, indicating insulin resistance decreases rapidly after birth. The

identified hormones are tumour necrosis factor-alpha (TNF-α), placental lactogen, placental growth hormone human chorionic somatomammotropin (HCS), cortisol, oestrogen, and progesterone (Clapp 2006; Devlieger 2008). HCS stimulates pancreatic secretion of insulin in the fetus and inhibits peripheral uptake of glucose in the mother (Lapolla 2005). If the pregnant woman's metabolism cannot compensate adequately for this, maternal hyperglycaemia results.

Maternal hyperglycaemia of varying degrees of severity has short- and long-term health implications for the woman and her baby. For the woman, these include a higher risk of developing gestational hypertension and pre-eclampsia during her pregnancy, having an increased risk of induction of labour, preterm birth, caesarean section, perineal trauma, postpartum haemorrhage (Crowther 2005; HAPO 2008; McCance 2011; NICE 2015), and a significant long-term risk of developing cardiovascular disease with half the women with GDM at risk of developing type 2 diabetes within five to 10 years (Bellamy 2009; Garrison 2015). Health implications for the baby include an increased risk of being born macrosomic and large-for-gestational age (Ornoy 2005; Young 2013), birth trauma (e.g. shoulder dystocia, bone fractures and nerve palsy) (Athukorala 2010), hyperbilirubinaemia (Harris 1997; Hedderson 2006), respiratory distress syndrome (Landon 2009) and neonatal hypoglycaemia (Devlieger 2008; Harris 2013). Neonatal hypoglycaemia may be associated with developmental delay in childhood (Lucas 1988), and, if prolonged or severe, may cause brain injury. Long-term health risks include higher rates of obesity, development of type 2 diabetes in childhood (Page 2014) and late onset diabetes, hypertension, and cardiovascular disease in adulthood (Ornoy 2011).

Description of the interventions

Effective interventions for treatment of GDM aim to reduce the risks of GDM for the mother and baby by normalising maternal glycaemia through treating maternal hyperglycaemia (Farrar 2017). Glucose control is usually measured by monitoring capillary blood glucose concentrations to ensure glucose concentrations are maintained within pre-defined glycaemic thresholds (Garrison 2015). This may be achieved through interventions such as the use of diet modifications (American Dietetic Association 2001; Ministry of Health 2014; NICE 2015), physical exercises (Harris 2005), pharmacological interventions such as oral hypoglycaemic medications or subcutaneous insulin (ACOG 2013; Ministry of Health 2014; NICE 2015), nutraceuticals (Thomas 2005; Hui 2009; Bagchi 2015) or other dietary supplements (D'Anna 2015; Paivaa 2015).

Different types of diet

The main treatment recommended for women with GDM is dietary modification (Bonomo 2005; Crowther 2005; Landon 2009; Ministry of Health 2014; NICE 2015). Dietary advice is aimed at preventing maternal hyperglycaemia and ensuring the woman's diet provides sufficient energy and nutrients to enable normal fetal growth while avoiding accelerated fetal growth patterns, and minimising excessive maternal weight gain (Dornhorst 2002). The recommendation is that all women diagnosed with GDM need to consult with a diabetic specialised dietitian or experienced nutritionist to determine the appropriate individualised diet, taking cultural preferences into account (Cheung 2009; Serlin 2009).

Different types of diets recommended for treatment include low or moderate glycaemic index (GI) diets, high fibre or high-fibre enriched diets, energy restricted diets, low carbohydrate diet or high complex carbohydrate diet and/or low monounsaturated fat diets (Rae 2000; Zhang 2006; Radesky 2008; Wolff 2008; Cheung 2009; Moses 2009; Louie 2011; Moreno-Castilla 2013; Asemi 2014b; Hernandez 2014; Viana 2014; Jamilian 2015; Ma 2015; Markovic 2016; NICE 2015).

Physical activity

It is unusual for GDM treatment recommendation to advise any physical activity modification alone. There are some trials evaluating the effects of physical exercises for women with GDM or type 2 diabetes. Physical exercises are usually recommended as low-impact activities, such as walking, swimming, stationary cycling, or special exercise classes for pregnant women (Davenport 2008; Mottola 2008; de Barros 2010; Manders 2010; Barakat 2012; Stafne 2012; ACOG 2015; Garrison 2015; Padayachee 2015).

Combined dietary modification and exercise

While often the initial treatment recommendation for women diagnosed with GDM is diet modification, it is common in clinical practice to combine this with exercise advice during pregnancy (ACOG 2013; Ministry of Health 2014; Garrison 2015; NICE 2015). This is often referred to as dietary and lifestyle advice (Artal 2007) or lifestyle modification programmes (LMP) where women participate in a comprehensive program on nutrition, exercise, and appropriate weight gain in pregnancy (Harris 2005; Cheung 2009; Shirazian 2010).

Pharmacological hypoglycaemic agents

Oral hypoglycaemic agents

When glycaemic treatment targets are unable to be achieved, pharmacological hypoglycaemic agents may be considered. While this traditionally has meant subcutaneous insulin for the woman with GDM, there has been an increase in the use of oral pharmacological hypoglycaemic agents as an alternative (Tieu 2010; Ogunyemi 2011). Oral agents have lower costs, are easier to administer and have greater acceptability for women with GDM (Ryu 2014). The most commonly used oral agents are sulphonylureas, which include acetohexamide, chlorpropamide, tolazamide, tolbutamide (first generation, usually not used to treat women with GDM) and glyburide (glibenclamide), glipizide and glimepiride (second generation) (Holt 2014; Kalra 2015); and biguanide (metformin) (Cheung 2009; Simmons 2015). Other oral hypoglycaemic agents used less frequently include alpha-glucosidase inhibitors (acarbose and miglitol) (Kalra 2015); thiazolidinedione's (TZDs) (pioglitazone and rosiglitazone) and meglitinides (repaglinide and nateglinide) (Kavitha 2013).

Trials have compared different oral pharmacological hypoglycaemic agents with each other or with placebo or with subcutaneous insulin and/or physical exercise and different diets (Langer 2000; Bertini 2005; Moretti 2008; Cheung 2009; Balsells 2015; Carroll 2015; Casey 2015).

Despite the wide use of oral pharmacological hypoglycaemic agents, these are not licensed for use during pregnancy in many countries (including the USA, UK, Australia, New Zealand) (Berggren 2013). This is due to the concern that they can cross the placenta, in particular the first-generation oral hypoglycaemic agents. At this stage, randomised controlled trials conducted with glyburide (second-generation sulphonylureas) and biguanide(metformin) have not demonstrated short-term harm to the mother or her growing baby (Langer 2000; Bertini 2005; Blumer 2013; Kelley 2015), but the information on long-term safety of these drugs remains limited.

Insulin

Women with GDM, who have difficulty controlling their glucose concentrations with lifestyle changes, such as diet and exercise, with or without the addition of an oral pharmacological agent require insulin (Mpondo 2015). Human insulin does not cross the placenta in clinically significant amounts and therefore is considered safe for the fetus when administered subcutaneously in pregnancy (Menon 1990; ADA 2015; Garrison 2015; Kelley 2015). Subcutaneous exogenous insulin is designed to mimic the

physiological secretion of endogenous insulin (Magon 2014; Home 2015). Some studies with insulin analogues indicate that they can cross the placenta when they form an antigen-antibody complex with immunoglobulins, which can carry the insulin analogues though the placenta (Jovanovic 2007, Durnwald 2013; Lv 2015).There is a need for large randomised controlled trials to establish the safe use in pregnancy of long-acting insulin analogues (glargine and detemir), as the effect of the transplacental insulin bound IgA's is unclear (Balsells 1997; Negrato 2012; Durnwald 2013). While fetal macrosomia has been identified in some observational and randomised controlled studies of long-acting insulin analogues, other concerns, including fetal death, have been raised (Gamson 2004; Negrato 2012; Coiner 2014).

There are several methods of administering insulin analogues. Historically and currently, they have been administered subcutaneously as a basal-bolus regimen (given prior to each meal) as this provides the most effective glycaemic control (Nachum 1999; Cheung 2009). These daily multiple subcutaneous injections may include rapid- (lispro, aspart, glulisine), intermediate- (neutral protamine hagedorn (NPH)) and long-acting (glargine and detemir) insulin analogues (Singh 2007; Horvath 2010). Fast-acting and intermediate-acting insulin analogues are currently the preferred choice of treatment for women with GDM as there is only limited data available for long-acting insulin in pregnancy (Jovanovic 2007; Durnwald 2013).

An alternative insulin administration method is via a continuous subcutaneous insulin infusion pump (CSII). Modern pumps are small and lightweight, battery operated and hold enough insulin for several days, which means frequent daily injections are not required. CSII pumps aim to maintain the basal rate of insulin, reducing the risk of maternal hypoglycaemia and decreasing the risk of fasting hyperglycaemia and are not associated with worse maternal and perinatal outcomes (Simmons 2001; Secher 2010; Bernasko 2012; Kesavadev 2016). Women using a CSII pump during their pregnancy for GDM and T2DM treatment preferred the flexible lifestyle with comparable healthcare costs (Gabbe 2000; Gonalez 2002; Wollitzer 2010).

Oral and nasal insulin are other alternatives to subcutaneous insulin and are currently under development because of their convenience, quick liver absorption and potentially avoiding adverse effects of weight gain and hypoglycaemia (Woodley 1994; Wang 1996; Carino 1999; Arbit 2004; Iyer 2010; Heinemann 2011; Fonte 2013). Although some pharmaceutical companies have stopped developing inhaled (nasal) insulin, some trials are still ongoing (Hompesh 2009; Rosenstock 2009;

Hollander 2010). It must be noted that research trials for oral and nasal insulin do not include women with GDM at this stage but are being considered for future research.

Other interventions

Other interventions reported in the literature for preventing GDM or treating women with GDM include dietary supplements and nutraceuticals. The term nutraceutical was created by Dr Stephen DeFelice, chairperson of the Foundation for Innovation in Medicine in 1989, who combined the terms nutrition and pharmaceutical. Nutraceuticals are marketed as nutritional supplements and sold with the intent to treat or prevent disease (Brower 1999; Gupta 2010; LakshmanaPrabu 2012). They are not governmentally regulated or licensed (Zeisel 1999; Rajasekaran 2008). Currently over 470 nutraceutical products are available with reported health benefits (Brower 1999; Eskin 2005; Gupta 2010). While randomised controlled trials involving nutraceuticals are scant in the literature for the treatment or prevention of GDM, there is some evidence from mainly observational studies. Dietary fibres from psyllium has been used for glucose control and reducing lipid levels in hyperlipidaemia (Hamid 2000; Baljit 2007; Rajasekaran 2008; Babio 2010). Omega-3 fatty acids have been suggested to reduce glucose tolerance for humans predisposed to diabetes, as insulin is required for synthesis of the long chain n-3 fatty acids (Sirtori 2002). The omega-3 fatty acid docosahexaenoic acid (DHA) involved with regulating insulin resistance has been recommended for women with GDM (Coleman 2001; Sirtori 2002; Thomas 2006; Gupta 2010). Magnesium has been shown to improve insulin sensitivity in non-diabetic participants (Guerrero-Romer 2004; Mooren 2011; Wang 2013), as has chromium picolinate (Broadhurst 2006; Martin 2006; Paivaa 2015), calcium and vitamin D (Dror 2011; Burris 2012; Poel 2012; Asemi 2014a; Burris 2014). Cinnamon and extracts of bitter melon may have some effect as co-treatments in the prevention of diabetes (Rajasekaran 2008; Hui 2009). Nutraceuticals should not be confused with the term dietary supplement, which is a product that is intended to supplement the diet that contains one or more ingredients such as vitamins, minerals, a herb, an amino acid or a concentrate, metabolite, constituent, extract or combinations of these (Rajasekaran 2008).

Myo-inositol, an isomer of inositol, is a dietary supplement of naturally occurring sugar commonly found in cereals, corn, legumes, and meat. Small randomised studies of low quality have shown a potential beneficial effect on improving insulin sensitivity and suggests that myo-inositol may be useful for women in preventing GDM but not for treatment of GDM (Facchinetti 2013; Malvasi 2014; Crawford 2015b; D'Anna 2015).

How the interventions might work

Treatment for women with GDM aims to normalise maternal fasting and postprandial glucose concentrations and modify fetal physiological responses to maternal hyperglycaemia, thereby reducing maternal and associated fetal and neonatal short-term morbidity. Two large randomised trials (Crowther 2005; Landon 2009) demonstrated reductions in birthweight and large-for-gestational-age infants in women with GDM who received treatment compared with women with GDM who were not treated. Any intervention that helps normalises maternal glucose concentrations therefore may be a useful treatment for women with GDM.

Human insulin stimulates glucose and amino acid uptake from the blood to various tissues and stimulation of anabolic processes for glycogen, protein, and lipid synthesis. Glucagon has opposing effects, causing release of glucose from glycogen, release of fatty acids from stored triglycerides and stimulation of gluconeogenesis. Metabolic homeostasis is maintained by the balance between insulin and glucagon (Wahlqvist 1978; Bantle 1983).

Different types of diet

One of the aims of dietary advice for women with GDM is to prevent maternal hyperglycaemia. Different types of diets recommended for treatment include low or moderate GI diets, high fibre or high-fibre enriched diets, energy restricted diets, low carbohydrate diet or high complex carbohydrate diet and/or low monounsaturated fat diets.

Carbohydrates absorbed following digestion are converted into glucose (Wahlqvist 1978; Bantle 1983). Current recommendations for women with GDM are for carbohydrate-controlled and low-GI diets, evenly distributed throughout the day, when remaining within the recommended glucose treatment targets (Clapp 2002; Dornhorst 2002; Ludwig 2002). Glycaemic index quantitatively defines the effect of carbohydrate-based foods on glucose concentrations (Foster-Powell 2002). Consumption of carbohydrates triggers the release of insulin and inhibits secretion of glucagon. Glucagon stimulates gluconeogenesis and release of the newly formed glucose from the liver into the blood. These actions produce a rapid return to fasting blood glucose levels and storage of glucose as glycogen or lipid (Kershaw 2006; Duncan 2007).

Likewise, a protein-rich meal leads to the release of insulin and glucagon. This rise of insulin associated with the protein meal stimulates uptake of the glucose formed in the liver by muscle and fat tissue (Nuttall 1984; van Loon 2000).

Other different types of diets such as fat (polyunsaturated fatty acids may be protective against impaired glucose tolerance, while saturated fatty acids can increase glucose and insulin concentrations) and soluble fibre (which may lower blood cholesterol by binding to it bile acids) are also thought to influence blood glucose concentrations (Zhang 2006; Babio 2010; Kim 2010).

Physical activity

Physical activity results in shifting fuel usage by the working muscle from primarily non-esterified fatty acids (NEFAs) to a blend of NEFAs, glucose, and muscle glycogen and improves insulin sensitivity in skeletal muscle and glucose control (Sigal 2004; Asano 2014). Glucose enters skeletal muscle cells via facilitated diffusion through a glucose transporter (GLUT4) and peripheral clearance of glucose in skeletal muscle depending on the blood flow to muscle through glycolysis and glycogenesis (Sakamoto 2002; Rose 2005; Richter 2013). Translocation of the GLUT4 transporter is induced by insulin and insulin-independent mechanisms (Richter 2001; Sigal 2004; Richter 2013). The improvements in insulin sensitivity after regular and sustained exercise, which improves blood supply to active skeletal muscle, include a decrease of insulin secretion and an increase of glucagon (Coderre 1995; Wojtaszewski 2002; Sigal 2004; Clapp 2006).

Oral hypoglycaemic agents

Second-generation sulphonylureas such as glyburide (glibenclamide), glipizide and glimepiride (Holt 2014; Kalra 2015) work by lowering glucose concentration through stimulating the release of insulin by binding to specific receptors in pancreatic β cell plasma membrane (Simonson 1984; Groop 1987; Groop 1991). First-generation sulphonylureas have been identified in the literature as crossing the placenta, being secreted in breast milk and have been associated with prolonged neonatal hypoglycaemia (Kemball 1970; Christesen 1998). Second-generation sulphonylureas are reported in the literature as less likely to cross the placenta (Elliott 1991; Langer 2000; Kraemer 2006; Cheung 2009; Schwartz 2013; Kalra 2015).

Biguanide (metformin) increases insulin sensitivity through the rate of hepatic glucose production, hepatic glycogenolysis and by increasing insulin-stimulated uptake of glucose in skeletal muscles (Sirtori

1994; Langer 2007; Cheung 2009; Kavitha 2013; Kalra 2015; Simmons 2015). This process reduces insulin resistance. Biguanide does not stimulate the fetal pancreatic β cells to produce insulin and hence is not associated with neonatal hyperinsulinaemia (Sirtori 1994; Ho 2007; Kavitha 2013).

Alpha-glucosidase inhibitors (acarbose and miglitol) reduce postprandial hyperglycaemia by slowing the absorption of carbohydrates in the intestines (Lebovitz 1997; Ho 2007; Kalra 2015). The effects of alpha-glucosidase inhibitors have not been studied well in pregnancy. Animal studies suggest that alpha-glucosidase inhibitors are not teratogenic (Young 2009; Holt 2014; Kalra 2015; Simmons 2015).

Thiazolidenediones (pioglitazone and rosiglitazone, Kavitha 2013) activate the peroxisome proliferator-activated receptor (PPAR) (a group of nuclear receptor proteins) reducing insulin resistance (Young 2009). The pharmacodynamics of these drugs are similar to glyburide (a second-generation sulphonylurea). Thiazolidenediones are bound to plasma proteins (99.8 %) and are metabolised in the liver (Stumvoll 2003; Langer 2007). While it appears that thiazolidinediones are not teratogenic, a high risk of placental transfer and an association with fetal death and growth restriction have been reported (Chan 2005; Holt 2014).

Meglitinides (repaglinide and nateglinide, Kavitha 2013) act similarly to sulphonylurea but use different receptors by stimulating the pancreas to release insulin in response to a meal. They block ATP-dependent potassium channels in functioning pancreatic β cells leading to the opening of calcium channels resulting in an influx of calcium. Increased intracellular calcium initiates and enhances insulin secretion (Rendell 2004; Kavitha 2013). Meglitinides agents have only been studied in non-pregnant T2DM participants showing some improvements with postprandial glycaemic results and HbA1c (Goldberg 1998; Rosenstock 2004). At this stage, meglitinides cannot be recommended for use in pregnancy (Kavitha 2013).

Insulin

Human insulin is a pancreatic hormone (secreted by the β cells of the pancreatic islets of Langerhans) that regulates the movement of glucose from blood into cells. Insulin lowers glucose concentration by stimulating peripheral glucose uptake and by inhibiting glucose production and release by the liver. Insulin inhibits lipolysis, proteolysis and gluconeogenesis and increases protein synthesis and conversion of excess glucose into fat (Kersten 2001; Wilcox 2005; Proud 2006). Treatment with exogenous subcutaneous insulin for women with GDM aims to achieve as close as possible

physiological profile by mimicking the pancreatic basal insulin release. However, this is based on average plasma insulin profiles and it is difficult to factor in the individual variability of absorption, dietary intake, and exercise (Hartman 2008; Grunberger 2013; Pagliuca 2014). Insulin treatment for women with GDM can include short- or rapid- (lispro, aspart, glulisine) and intermediate- and long acting- (neutral protamine hagedorn (NPH), glargine, detemir) insulin analogues (Singh 2007; Horvath 2010; Pollex 2011; Ansar 2013; Magon 2014) given usually by daily multiple or single subcutaneous injections guided by recommended glycaemic targets. Table 2.1 identifies how the different subcutaneous insulin analogues act to achieve a more physiological profile. Please note that some studies results cited in Table 2.1 are for pregnant women who have either T1DM or T2DM only. More studies are needed that include women with GDM.

Table 2.1:Type of subcutaneous insulin and action towards achieving a physiological profile

Type of Insulin	Action
Short- and rapid-acting insulin	
Lispro	Amino acid substitutions (inverting lysine at position 28 and proline at position 29 on the β-chain of the insulin molecule), monomeric in tissues (Magon 2014; Home 2015). Peak insulin action achieved within 1 hour after injection and duration of action 2 to 4 hours (Durnwald 2008). Antibody levels not increased over those seen with regular human insulin. Does not seem to cross the placenta (Jovanovic 2007).
Aspart	Amino acid substitutions (proline at position 28 on the β-chain of the insulin molecule with negatively charged aspartic acid), monomeric in tissues (Magon 2014; Home 2015). Peak action 31-70 minutes for 2 to 4 hours and lowers postprandial glucose levels significantly better than human insulin (Jovanovic 2007; Magon 2014). No evidence that insulin aspart is teratogenic (Hod 2005).
Glulisine	Amino acid substitutions and reformulation, rapidly monomeric in tissues (Home 2015). Produces peak blood glucose level at 15-20 minutes and lowers postprandial glucose levels significantly better than human insulin (Jovanovic 2007). Adverse effects on embryo-fetal development were only seen at animal maternal toxic dose levels inducing hypoglycaemia. No clinical data currently available for the use of Insulin glulisine in pregnancy (Magon 2014).
Intermediate- and long-acting insulin	
Neutral Protamine Hagedorn (NPH)	Protamine crystal suspension (Home 2015). NPH has an onset of action approximately after 90 minutes and a duration of action up to 16 to 18 hours (Jovanovic 2007; Magon 2014). No randomised controlled trials currently to confirm safety during pregnancy but several case reports and one case-control study indicate no fetal morbidity or macrosomia (Magon 2014).
Detemir	Slowly absorbed and binds to albumin through a fatty-acid chain attached to the lysine at residue B29 resulting in reduction in its free level which slows distribution to peripheral target tissues with a duration of action of up to 24 hours (Magon 2014). Significant improvement in fasting plasma glucose with insulin detemir during pregnancy for T1DM without an increased incidence of hypoglycaemia, including at night. No adverse maternal or neonatal effects were identified (Mathiesen 2012; Callesen 2013; Hod 2014). Suffecool 2015 conducted a small study including 11 women with GDM and five women with type 2 diabetes receiving detemir assessing maternal and cord blood at birth. The results showed that while maternal detemir levels were in the expected range for adults, the hormone was undetectable in the cord blood, indicating that detemir does not cross the human placenta. Larger studies and randomised controlled trials are needed to confirm.
Glargine	Slowly absorbed and replaces the human insulin amino acid asparagine at position A21 of the A chain with glycine and two arginine molecules are added to one end (C-terminal) of the B-chain with onset of action approximately after 90 minutes of injection and lasting for about 24 hours (Price 2007; Ansar 2013). Studies in non-pregnant participants have indicated that insulin glargine has a smooth peak-free profile of action, with a reduced incidence of nocturnal hypoglycaemia and better glycaemic control (Woolderink 2005, Graves 2006; Magon 2014). Concerns regarding insulin glargine's use in pregnancy are raised from case-control, case reports and retrospective studies (including women with T1DM, T2DM and some with GDM) that have shown six- to eight-fold increased affinity for insulin growth factor (IGF)-1 receptor compared with human insulin. However, results of these studies found no association with increased fetal macrosomia or neonatal morbidity with the use of glargine in pregnancy (Bolli 2000; Pöyhönen-Alho 2007; Egerman 2009; Lv 2015). No randomised controlled trials currently to confirm safety during pregnancy.

Other interventions

Supplemental nutraceuticals are believed to support the chemical food elements (nutrients) needed for the human body's metabolism and prescribed when there is a diagnosis of a nutrient depletion or required for strengthening the metabolism or prevention of disease (LakshmanaPrabu 2012). Currently there are over 470 nutraceuticals available including supplements for GDM (Eskin 2005; Gupta 2010). The mechanism of action for nutraceuticals and other dietary supplements are often not clear and further high-quality research is needed.

Myo-inositol is required for cell membrane formation and works on the insulin receptors of each cell, so insulin can bind effectively thus reducing insulin resistance (Croze 2013). It is involved with mediating the pathway of intracellular insulin signals increasing cellular effectiveness of insulin within the cell (Larner 2010). Small randomised trials of low quality conducted in Italy have shown some effect in preventing GDM (D'Anna 2013; Facchinetti 2013; Malvasi 2014; D'Anna 2015). Further high-quality research is needed to establish if myo-inositol improves health outcomes for mothers and their babies.

Why it is important to do this overview

There are several Cochrane systematic reviews regarding treatments for women with GDM. These include different types of diet, exercise, subcutaneous insulin, oral hypoglycaemic agents and other oral supplements as well as management recommendations such as induction of labour, caesarean section, antenatal breast milk expression and blood glucose monitoring. This makes it difficult for clinicians, consumers and guideline developers to easily interpret the available information. A Cochrane overview of systematic reviews would provide summary evidence of the effective on relevant health outcomes of different treatments for women with GDM as a one-stop resource for health professionals, consumers and guideline developers aiding the simplifying of clinical treatment decision-making and assisting with the process of guideline development.

2.2.2 Objectives

The objective of this overview is to provide a comprehensive synthesis of evidence from randomised controlled trials in relevant published Cochrane systematic reviews of interventions for treating women with GDM and their effects on important health outcomes relevant to women with GDM and their babies, and to report any adverse effects associated with these treatments. A further aim is to identify specific significant research gaps requiring further primary research of treatment for women with GDM.

2.2.3 Methods

The methodology for data collection and analysis is based on Chapter 22 (Overviews of Reviews) of the *Cochrane Handbook of Systematic Reviews of Interventions* (Becker 2011). Only published Cochrane systematic reviews of randomised controlled trials focusing on treatments for women with GDM were considered in this overview noting their publication and search dates. We did not attempt to update individual Cochrane systematic reviews that were due for updates (two years since publication).

We contacted the Cochrane Pregnancy and Childbirth group to identify any relevant new reviews and review updates that were being undertaken and/or near completion for inclusion of the most up-date versions of reviews. Cochrane protocols and title registrations for interventions for women with GDM were identified through the same process to identify future inclusions and were classified as *ongoing Cochrane systematic reviews*. They will be considered for inclusion in the update of this overview.

Similarly, reviews with pre-specified overview outcomes but with no outcome data (either no studies found or women with GDM did not feature in the included trial(s)) were classified as *reviews awaiting classification* and will be added to this overview when future up-dates if the reviews include relevant data.

Criteria for considering reviews for inclusion

Participants

The participants in the Cochrane systematic reviews were women diagnosed with GDM receiving any form of treatment for GDM (as identified by the review). Women with type 1 and type 2 diabetes were excluded.

Interventions

We considered all treatments for women with GDM including:

- Any dietary modifications (including low-moderate GI diet, high-moderate GI diet, energy-restricted diet, no energy restricted diet, DASH diet (Dietary Approaches to Stop Hypertension), low-carbohydrate diet, high-carbohydrate diet, high unsaturated fat diet, low unsaturated fat diet, low GI diet, high fibre moderate GI diet, soy protein-enriched diet, high fibre diet, ethnic-specific diet).

- Any physical exercises (including brisk walking, resistance exercises, circuit workouts, elastic band exercises, any form of bicycling, low-intensity aerobic exercises, home-based exercises, mindfulness yoga).
- Pharmacological interventions (oral hypoglycaemic agents including metformin, glibenclamide, acarbose, tolbutamide, chlorpropamide or combination of these therapies or subcutaneous insulin).
- Nutraceuticals or other dietary supplements (including myo-inositol).
- Other interventions as identified by included reviews (including glycaemic treatment targets for GDM, management of labour and birth for women with GDM, lifestyle interventions).

For further description of possible interventions see under ‘Description of the interventions’ on page 31.

Outcomes

The outcomes for this overview review were agreed by consensus of authors of Cochrane systematic reviews relating to GDM (Bain 2016), including the outcomes that were used in the 'Grading of Recommendations Assessment, Development and Evaluation' (GRADEpro).

Primary outcomes

Maternal

- Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia as defined in reviews).
- Caesarean section.
- Development of type 2 diabetes.

Neonatal

- Perinatal (fetal and neonatal death) and later infant mortality.
- Large-for-gestational age (as defined in reviews).
- Death or serious morbidity composite (as defined in reviews, e.g. perinatal or infant death, shoulder dystocia, bone fracture or nerve palsy).
- Neurosensory disability in later childhood (as defined in reviews).

Secondary outcomes

Maternal

- Use of additional pharmacotherapy.
- Maternal hypoglycaemia (as defined in the reviews).
- Glycaemic control during/end of treatment (as defined in the reviews).
- Weight gain in pregnancy.
- Adherence to the intervention.
- Induction of labour.
- Placental abruption.
- Postpartum haemorrhage (as defined in the reviews).
- Postpartum infection.
- Perineal trauma/tearing.
- Breastfeeding at discharge, six weeks postpartum, six months or longer.
- Maternal mortality.
- Sense of well-being and quality of life.
- Behavioural changes associated with the treatment.
- Women's view of the intervention.
- Relevant biomarker changes associated with the intervention (including adiponectin, free fatty acids, triglycerides, high-density lipoproteins, low-density lipoproteins, insulin).

Maternal long-term outcomes

- Postnatal depression.
- Body mass index (BMI).
- Postnatal weight retention or return to pre-pregnancy weight.
- Development of type 2 diabetes.
- Impaired glucose tolerance.
- Subsequent gestational diabetes.
- Cardiovascular health (as defined in the reviews including blood pressure, hypertension, cardiovascular disease, metabolic syndrome).

Fetal/neonatal outcomes

- Stillbirth.
- Neonatal death.
- Macrosomia (greater than 4000 g; or as defined in the reviews).
- Small-for-gestational age (as defined in the reviews).
- Birth trauma (e.g. shoulder dystocia, bone fracture, nerve palsy).
- Gestational age at birth.
- Preterm birth (< 37 weeks' gestation and < 32 weeks' gestation).
- Five-minute Apgar < 7.
- Birthweight and z score.
- Head circumference and z score.
- Length and z score.
- Ponderal index.
- Adiposity (including skinfold thickness measurements (mm), fat mass).
- Neonatal hypoglycaemia (as defined in the reviews).
- Respiratory distress syndrome.
- Neonatal jaundice (hyperbilirubinaemia) (as defined in the reviews).
- Hypocalcaemia (as defined in the reviews).
- Polycythaemia (as defined in the reviews).
- Relevant biomarker changes associated with the treatment (including insulin, cord c-peptide).

Later infant/childhood outcomes

- Weight and z scores.
- Height and z scores.
- Head circumference and z scores.
- Adiposity (including BMI, skinfold thickness, fat mass).
- Educational attainment.
- Blood pressure.
- Development of type 1 diabetes.
- Development of type 2 diabetes.
- Impaired glucose tolerance.

- Dyslipidaemia or metabolic syndrome.

Child as an adult outcomes

- Weight and z scores.
- Height and z scores.
- Adiposity (including BMI, skinfold thickness, fat mass).
- Cardiovascular health (as defined in the reviews including blood pressure, hypertension, cardiovascular disease, metabolic syndrome).
- Employment, education and social status/achievement.
- Dyslipidaemia or metabolic syndrome.
- Development of type 1 diabetes.
- Development of type 2 diabetes.
- Impaired glucose tolerance.

Health service use

- Number of antenatal visits or admissions.
- Number of hospital or health professional visits (including midwife, obstetrician, physician, dietician, diabetic nurse).
- Admission to neonatal intensive care unit/nursery.
- Length of stay in neonatal intensive care unit or special care baby unit.
- Length of antenatal stay.
- Length of postnatal stay (maternal).
- Length of postnatal stay (baby).
- Cost of maternal care.
- Cost of neonatal/child/adult care.
- Costs associated with the treatment.
- Costs to families associated with the treatment (e.g. change of diet, extra antenatal visits, etc).

For Cochrane systematic reviews to be eligible for inclusion in this overview review, a review had to pre-specify some or all of the overview primary and secondary outcomes and have reported data for treatments for women with GDM from at least one included trial.

Cochrane systematic reviews that had pre-specified some or all of the overview outcomes, but had no reported data or no included trials, have been listed as *reviews awaiting for further classifications* and will be re-considered in future up-dates of this overview review.

Search methods for identification of reviews

We searched the *Cochrane Database of Systematic Reviews* on 28 June 2017 using the term 'gestational diabetes' with the T*itle, Abstract, Keywords* and the *'all text'* function and identified from this search which reviews, and protocols related to treatment for women with GDM. We did not apply any language or date restrictions.

Data collection and analysis

Cochrane systematic reviews published addressing any treatments for women diagnosed with GDM were selected. Reviews and studies including treatment for pregnant women with known Type I and Type II diabetes were excluded. The methodology for data collection was based on Chapter 22 of the of the *Cochrane Handbook of Systematic Reviews of Interventions* (Becker 2011). Where appropriate the overview was prepared using the Review Manager Software (RevMan 2014).

Selection of reviews

Three overview authors independently assessed all potential Cochrane systematic reviews for inclusion identified through the search. We resolved any disagreements through discussions.

Data extraction and management

Two overview review authors, not involved in the included Cochrane systematic reviews, independently extracted data using a pre-defined data extraction form. We resolved any discrepancies through discussion. Where any information from the reviews were unclear or missing, we contacted the review authors (see under heading Methods page 54).

Information from included reviews was extracted on the following:

- Population demographics: We summarised participant's characteristics with inclusion and exclusion criteria as reported in the included reviews.
- Review characteristics: We reported the number of included trials and trial countries, design and publication years, the number of participants (women, babies and children) in each review; the date

of search conducted for each review; up-to-date status (< two years was considered up-to-date); described the interventions and comparisons; included all pre-specified outcomes relevant to the overview and assessed and reported on the quality of the included Cochrane systematic reviews using the Cochrane risk of bias assessment as detailed in the included reviews.

- Statistical summary: We reported the statistical summary by outcomes.

Assessment of methodological quality of included reviews

Quality of included trials within reviews

We did not assess the quality of the trials within the included Cochrane systematic reviews but reported the trial quality according to the review authors assessments (Risk of bias assessments from included reviews). We also noted and reported for each included review the publication and search date (Table 2.4).

Quality of evidence in the included reviews

Two overview review authors not listed as authors in the included Cochrane systematic reviews independently extracted outcomes that had been assessed in the individual reviews using the GRADE approach. Where the relevant outcomes had not been assessed using the GRADE approach, these were assessed independently by the two overview review authors using 'Grading of Recommendations Assessment, Development and Evaluation' (GRADE) (Balshem 2011; GRADEpro).

GRADE Assessment

GRADEpro uses five criteria: study limitations (risk of bias), consistency of effect, imprecision, indirectness and publication bias to assess the quality of the body of evidence for pre-specified outcomes, as described in Chapter 5 of the GRADE Handbook. It rates the quality of evidence as either:

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

We reported the quality of evidence as assessed by the Cochrane systematic review authors.

Two overview review authors (RM, JB) generated 'Summary of findings tables' using GRADE for Cochrane systematic reviews included in the overview that did not produce a 'Summary of findings table' using GRADE. This applied for the reviews of Boulvain 2001 and Han 2012.

The following seven maternal, seven child (as neonate, child, adult) and seven heath service costs outcomes for quality assessment were agreed by consensus between the overview review authors and all other review authors of Cochrane systematic reviews relating to GDM (Bain 2016).

Maternal

1. Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia).
2. Caesarean section.
3. Development of type 2 diabetes.
4. Perineal trauma.
5. Return to pre-pregnancy weight.
6. Postnatal depression.
7. Induction of labour.

Child (as neonate, child, adult)

1. Large-for-gestational age.
2. Perinatal mortality.
3. Death or serious morbidity composite.
4. Neonatal hypoglycaemia.
5. Adiposity.
6. Diabetes.
7. Neurosensory disability.

Health service use

1. Number of antenatal visits or admissions.
2. Length of postnatal stay (mother).
3. Length of postnatal stay (baby) (including neonatal intensive care unit or special re baby unit).

4. Costs to families associated with the treatment.
5. Costs associated with the treatment.
6. Cost of maternal care.
7. Cost of child (as neonate, child, adult) care.

In order to provide a comprehensive judgement summary for outcomes, the overview review authors decided that *all* the overview secondary outcomes needed to be assessed for quality using the four GRADE quality ratings as above. This would provide a more accurate and comprehensive reporting of the evidence for a treatment intervention for women with GDM. These additional assessments were made by RM and JB.

Overall quality of the included reviews

We used two different quality measurement assessment tools for this overview in order to assess the overall quality of the included reviews: 'Assessment of Multiple Systematic Reviews' (AMSTAR) (Shea 2007; Shea 2009) and 'Risk of Bias in Systematic Reviews' (ROBIS) (Whiting 2016).

AMSTAR Assessment

Two overview authors not involved with the included Cochrane systematic reviews independently assessed the quality of the reviews using AMSTAR (A Measurement Tool to Assess Systematic Reviews). We resolved differences through discussion. The AMSTAR (Shea 2007; Shea 2009) tool is an instrument that measures 11 components to assess the methodological quality of a systematic review. Each AMSTAR domain is rated as:

- 'yes' (Y) (clearly done),
- 'no' (N) (clearly not done),
- 'cannot answer' (CA) or
- 'not applicable' (NA).

High-quality reviews score eight or higher, moderate-quality reviews score between four and seven and low-quality systematic reviews score three or fewer 'yes' answers.

AMSTAR score (out of 11 criteria)	Rating
8 to 11	high quality
4 to 7	moderate quality
3 or lower	low quality

The included Cochrane systematic reviews were assessed using the following AMSTAR questions:

1. Was an a **priori design** provided?
2. Was there **duplicate study** selection and data extraction?
3. Was a **comprehensive literature search** performed?
4. Was the **status of publication** (i.e. grey literature) used as an inclusion criterion?
5. Was a **list of studies** (included and excluded) provided?
6. Were the **characteristics of the included studies** provided?
7. Was the **scientific quality** of the included studies assessed and documented?
8. Was the scientific quality of the included studies used **appropriately in formulating conclusions?**
9. Were the **methods** used to combine the findings of studies appropriate?
10. Was the likelihood of **publication bias** assessed?
11. Was the **conflict of interest** included?

A score out of 11 is given regardless of any 'cannot answer' or 'not applicable' responses (https://amstar.ca/contact_us.php).

ROBIS Assessment

Two overview authors not involved with the included Cochrane systematic reviews independently assessed the quality of the reviews using ROBIS (Risk Of Bias In Systematic reviews) (Whiting 2016). We resolved differences through discussion.

ROBIS considers risk of bias across four key domains. Each domain elicits information about possible limitations of the included Cochrane systematic review through a series of questions. Domain 1 - 3 have 5 question each and Domain 4 has 6 questions. Questions are answered with either yes, no or unclear. The risk of bias for each domain is then judged and summarised as 'low, high or unclear concerns'. Once all four domains are assessed an overall judgement of risk of bias is made identified as 'low, high

or unclear risk' (Whiting 2016). The included Cochrane systematic reviews were assessed using the following ROBIS domains:

Domain 1: Study eligibility criteria.

Domain 2: Identification and selection of studies.

Domain 3: Data collection and study appraisal.

Domain 4: Synthesis and findings.

Data synthesis

A description of the characteristics of included Cochrane systematic reviews was undertaken (Table 2.4). We did not examine indirect comparisons and did not conduct a network meta-analyses. We summarised the results of the included Cochrane systematic reviews by categorising their findings in the following framework organised by overview review outcomes:

- Effective interventions: indicating that the review found high-quality evidence of effectiveness for an intervention.
- Promising interventions (more evidence needed): indicating that the review found moderate-quality evidence of effectiveness for an intervention, but more evidence is needed.
- Probably no difference between interventions: direction of effect suggests benefit/harm or ineffective, 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, more evidence needed.

This approach to summarising the evidence was based on the publication of Effective Care in Pregnancy and Childbirth (Vol. 2: Materials and methods used in synthesizing evidence to evaluate the effects of care during pregnancy and childbirth) (Chalmers 1989) and 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).

2.2.4 Results

Our search on 28 June 2017 of the *Cochrane Database of Systematic Reviews* identified 52 reviews and published protocols from 9706 records, four records from the Cochrane Pregnancy and Childbirth group's title registrations list, a total of 56 records (Figure 2.1). Following the screening of title and review abstracts we excluded 29 protocols and reviews as not eligible. The remaining 27 reviews, protocols and title registrations were assessed for eligibility. We excluded 15 publications which were either full-text reviews, protocols, or title registrations (Figure 2.1). These included one protocol (Pelaez-Crisologo 2015) that has been withdrawn, one report (Martis 2016b) was this overview protocol, two reviews were withdrawn as they were out-of-date (Walkinshaw 1996; Walkinshaw 2006), one review (Alwan 2009) has been superseded as it is now split into three new titles and published as one protocol (Brown 2016b) and two reviews (Brown 2017a; Brown 2017b), both reviews are included for assessment in this overview, one review (Ceysens 2006) has been superseded with a new title and is now published as a review (Brown 2017c), and is one of the included reviews for assessment and three reviews had no results for women with GDM for vitamins and other micronutrients (Vitamin D - DeRegil 2016; Vitamin A - McCauley 2015; Vitamin C - Rumbold 2015) (Table 2.2: *Characteristics of excluded reviews*). An additional three title registrations and three protocols, which indicated a treatment for women with GDM and have some or all pre-specified primary and secondary overview review outcomes were excluded at this stage and have been listed in Table 2.4 as *Ongoing reviews*. When they are published they will be considered for inclusion in future updates of this overview.

Figure 2.1: Search flow diagram

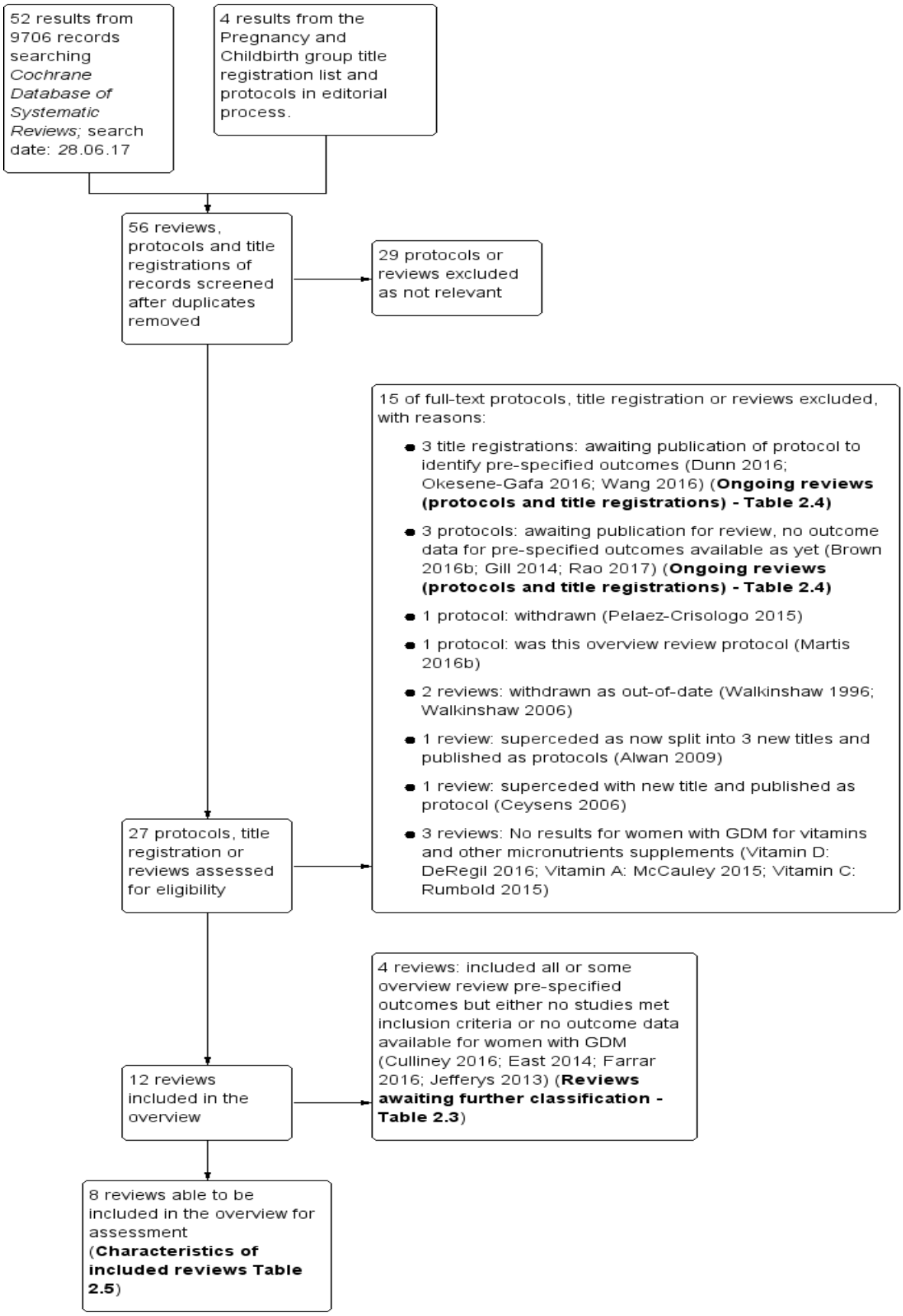


Table 2.2: Characteristics of excluded reviews

Review ID and title	Reason for exclusion
Alwan 2009 Treatments for gestational diabetes	Most pre-specified overview outcomes included but this review was too large and has now been split into three reviews. Two reviews are currently published as 'Oral anti-diabetic pharmacological therapies for the treatment of women with gestational diabetes' Brown 2017a and 'Lifestyle interventions for the treatment of women with gestational diabetes' (Brown 2017b) and are included reviews in this overview (Table 2.4: Characteristics of included reviews). The other one is currently published as a protocol entitled 'Insulin for the treatment of women with gestational diabetes' Brown 2016b (Table 2.2: Ongoing Cochrane systematic reviews). The reviews and the protocol include all overview pre-specified primary outcomes for maternal and neonatal outcomes and all overview pre-specified secondary outcomes for maternal, maternal long-term, fetal/neonatal, later infant/childhood, child as an adult and health services use.
Ceysens 2006 Exercise for diabetic pregnant women	This review, which included some of the pre-specified overview primary and secondary outcomes, was not up-to-date and has now been superseded with a new title. It is now published as 'Exercise for pregnant women with gestational diabetes for improving maternal and fetal outcomes' (Brown 2017c) (Table 2.4: Characteristics of included reviews) and is an included review in this overview for assessment.
DeRegil 2016 Vitamin D supplementation for women during pregnancy	Some primary and secondary overview review pre-specified outcomes included but not later infant/childhood, child as an adult and health service use outcomes. Pregnant women with pre-existing conditions (i.e. GDM) were excluded.
McCauley 2015 Vitamin A supplementation during pregnancy for maternal and newborn outcomes	Some overview review pre-specified outcomes included. Neonatal primary outcome: perinatal mortality; Maternal secondary outcomes: Postpartum infection and maternal mortality. Fetal/neonatal secondary outcomes: Stillbirth, preterm birth (< 37 weeks' gestation) and birthweight. No maternal long-term, later infant/childhood, child as an adult and health service use secondary outcomes. No outcome data for women with GDM separated out for the above outcomes.
Rumbold 2015 Vitamin C supplementation in pregnancy	Some overview review pre-specified outcomes included. Maternal primary outcome: Hypertensive disorder of pregnancy and Caesarean. Neonatal primary outcome: Death or serious morbidity composite and neurosensory disability; Maternal secondary outcomes: Postpartum haemorrhage, maternal mortality, and women's view of care. Fetal/neonatal secondary outcomes: Stillbirth, neonatal death, gestational age at birth, preterm birth (< 37 weeks' gestation), five-minute Apgar < 7, birthweight, respiratory distress syndrome and neonatal jaundice. No later infant/childhood, child as an adult and health service use secondary outcomes. Of the 29 studies included in this review five studies excluded women with any diabetes in pregnancy. No outcome data for women with GDM separated out for the above outcomes.
Walkinshaw 1996 Dietary regulation for gestational diabetes	Pre-specified outcomes not available as this review has been withdrawn and is now published as 'Different types of dietary advice for women with gestational diabetes mellitus' Han 2017, which is an included review in this overview review (Table 2.5: Characteristics of included reviews).
Walkinshaw 2006 Very tight versus tight control for diabetes in pregnancy	Pre-specified outcomes not available as this review has been withdrawn because it is out-of-date. The review team were unable to prepare the up-date and it is now included in the review currently published as 'different intensities of glycaemic control for women with gestational mellitus' Martis 2016a

A further four Cochrane systematic reviews (Culliney 2016; East 2014; Farrar 2016 and Jefferys 2013) (Figure 2.1) have been listed as *Cochrane systematic* r*eviews awaiting further classification* (Table 2.3). These reviews include some or all of the pre-specified primary and secondary overview outcomes but either had no studies that meet the inclusion criteria for that review or no outcome data were reported for women with GDM. These Cochrane systematic reviews will be considered for future up-dates of this overview.

Therefore, we included eight Cochrane systematic reviews in this overview reporting on 62 RCTs (9133 women, 8373 babies and 767 children) for assessment (Figure 2.1) See characteristics of included reviews (Table 2.5).

Table 2.3: Cochrane systematic reviews awaiting further classification

Review citation	Overview outcomes pre-specified in review with no outcome data	Main conclusion(s) of the review
Culliney KAT, Parry GK, Brown J, Crowther CA. Regimens of fetal surveillance of suspected large-for-gestational-age fetuses for improving health outcomes. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD011739. DOI: 10.1002/14651858.CD011739.pub2.	Overview maternal primary outcomes pre-specified include: Mode of birth (caesarean section). Overview neonatal primary outcomes pre-specified include: Perinatal (fetal and neonatal death) but not later infant mortality and death or serious morbidity composite (as defined in reviews, e.g. perinatal or infant death, shoulder dystocia, bone fracture or nerve palsy). Overview secondary outcomes pre-specified for maternal include: Induction of labour, perineal trauma, post-partum haemorrhage, breastfeeding and women's view of care. No maternal long-term secondary outcomes pre-specified. Secondary pre-specified outcomes for fetal/neonatal, later infant/childhood, child as an adult include: gestational age at birth, birthweight, and z-score, LGA, Apgar < 7, neonatal hypoglycaemia, birth length and HC and adiposity. Health services use outcomes pre-specified include: admission to neonatal special care unit or NICU.	No studies met the eligibility criteria for inclusion. Future review updates may include women with GDM. "Most of the cases of LGA infants are associated with maternal factors including maternal height, weight, body mass index (BMI), gestational weight gain, ethnicity, parity and maternal age, as well as the presence of pre-gestational or gestational diabetes". "There is no evidence from randomised controlled trials to evaluate regimens of fetal surveillance for suspected large-for-gestational age (LGA) fetuses to improve health outcomes".
East CE, Dolan WJ, Forster DA. Antenatal breastmilk expression by women with diabetes for improving infant outcomes. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No.: CD010408. DOI: 10.1002/14651858.CD010408.pub2.	No overview primary outcomes for maternal and neonatal outcomes pre-specified. Overview secondary pre-specified outcomes for maternal includes: breastfeeding at six months. No maternal long-term secondary outcomes pre-specified. Secondary outcomes pre-specified for fetal/neonatal include: gestational age at birth and neonatal hypoglycaemia. No later infant/childhood, child as an adult secondary outcomes pre-specified. Secondary outcomes pre-specified for health services use include: economic costs (as defined by trial authors) which may include some of the overview pre-specified outcomes	No studies met the eligibility criteria for inclusion. Future review updates may include women with GDM. "There were no published or unpublished randomised controlled trials comparing antenatal expressing with not expressing. One randomised trial is currently underway. There is no high level systematic evidence to inform the safety and efficacy of the practice of expressing and storing breast milk during pregnancy".

Review citation	Overview outcomes pre-specified in review with no outcome data	Main conclusion(s) of the review
Farrar D, Tuffnell DJ, West J, West HM. Continuous subcutaneous insulin infusion versus multiple daily injections of insulin for pregnant women with diabetes. Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD005542. DOI: 10.1002/14651858.CD005542.pub3.	All overview primary outcomes for maternal and neonatal outcomes pre-specified. All overview secondary outcomes for maternal, maternal long-term, fetal/neonatal, later infant/childhood, child as an adult and health services use pre-specified.	None of the included trials recruited women with GDM. Future review up-dates may include women with GDM. “There were no trials of appropriate methodological quality that assessed the use of MDI versus CSII for women with GDM” and suggest that as “prevalence of GDM is increasing and these women may require insulin; this is a group of women who should be included in future trials”. "Large multi-centre randomised, adequately powered trials are needed to assess the effectiveness of continuous subcutaneous insulin infusion compared with multiple daily injections for women with diabetes (GDM and pre-existing) in pregnancy who require insulin. It would be beneficial if outcomes were consistent across trials and included women’s preferences. Further trials to assess the effects of pumps on birthweight and macrosomia rates are needed. Future trials should undertake longer-term follow-up of participants (women and their infants) as well as assessment of associated costs".
Jefferys AE, Siassakos D, Draycott T, Akande VA, Fox R. Deflation of gastric band balloon in pregnancy for improving outcomes. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD010048. DOI: 10.1002/14651858.CD010048.pub2.	Overview primary outcome for maternal pre-specified include: Hypertensive disorder in pregnancy. No overview primary outcomes for neonatal are pre-specified. Overview secondary outcomes pre-specified for maternal include: maternal weight gain in pregnancy, maternal hospital antenatal and postnatal admissions. No overview secondary outcomes pre-specified for maternal long-term. Overview secondary outcomes pre-specified for fetal/neonatal include: Apgar score < 7 at 5 minutes, preterm birth < 37 weeks and < 28 weeks, birthweight, macrosomia, SGA, stillbirth and early neonatal death. No overview secondary outcomes pre-specified for later infant/childhood, child as an adult and health services use.	No studies met the eligibility criteria for inclusion. Future review up-dates may include women with GDM and gastric balloons. "At present, there is no guidance on the best management of a gastric band during pregnancy and there is variation in care. Some clinicians advocate leaving the balloon filled (inflated) to limit food intake and limit weight gain during pregnancy. This strategy might reduce the likelihood of maternal high blood pressure or gestational diabetes and so improve the outcomes for mother and baby".

Table 2.4: Ongoing Cochrane systematic reviews (Protocol and Title registrations)

Protocol ID and title registrations	Reference	Inclusion criteria for types of participants	Comparison interventions	Overview outcomes pre-specified in the protocols
Brown 2016b Insulin for the treatment of women with gestational diabetes (Protocol)	Brown J, Grzeskowiak L, Williamson K, Downie MR, Crowther CA. Insulin for the treatment of women with gestational diabetes. Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD012037. DOI:10.1002/14651858.CD012037	Women diagnosed with GDM. Pregnant women with type 1 or type 2 diabetes will be excluded	Comparing any insulin with oral anti-diabetic agents or diet or exercise or diet plus exercise or other treatments not identified above or comparing one type of insulin with another type or one insulin regimen with another insulin regimen.	All overview primary outcomes for maternal and neonatal outcomes pre-specified. All overview secondary outcomes for maternal, maternal long-term, fetal/neonatal, later infant/childhood, child as an adult and health services use pre-specified.
Gill 2014 Home versus hospital glucose monitoring for gestational diabetes during pregnancy (Protocol)	Gill MG, Nguyen TMN, Bain E, Crowther CA, Middleton P. Home versus hospital glucose monitoring for gestational diabetes during pregnancy. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD011069. DOI:10.1002/14651858.CD011069	Women diagnosed with GDM and of any age, gestation and parity will be included. Pregnant women with type 1 or type 2 diabetes will be excluded.	Comparing all home care in glucose monitoring with hospital care.	Maternal primary outcome pre-specified include: Mode of birth (caesarean section) Neonatal primary outcomes pre-specified include: Perinatal (fetal and neonatal death) and late infant mortality and large for gestational age (as defined in reviews) Secondary outcomes pre-specified for maternal include: Use of additional pharmacotherapy, glycaemic control during/end of treatment (as defined in the reviews), weight gain in pregnancy, adherence to the intervention, induction of labour, placental abruption, postpartum haemorrhage (as defined in the reviews), postpartum infection, perineal trauma/tearing, maternal mortality, sense of well-being and quality of life. Secondary outcomes pre-specified for maternal long-term include: Body mass index (BMI), postnatal weight retention or return to pre-pregnancy weight, development of type 1 diabetes, development of type 2 diabetes, impaired glucose tolerance, subsequent gestational diabetes.

Protocol ID and title registrations	Reference	Inclusion criteria for types of participants	Comparison interventions	Overview outcomes pre-specified in the protocols
				Secondary outcomes pre-specified for fetal/neonatal include: Stillbirth, neonatal death, small-for-gestational age (as defined in the reviews), birth trauma (e.g. shoulder dystocia, bone fracture, nerve palsy), gestational age at birth, preterm birth (< 37 weeks' gestation and < 32 weeks' gestation), five-minute Apgar < 7, birthweight and z score, ponderal index, neonatal hypoglycaemia (as defined in the reviews), respiratory distress syndrome, neonatal jaundice (hyperbilirubinaemia) (as defined in the reviews). Secondary outcomes pre-specified for later infant/childhood include: Weight and z scores, height and z scores, adiposity (including BMI, skinfold thickness, fat mass), development of type 1 diabetes, development of type 2 diabetes, impaired glucose tolerance, dyslipidaemia or metabolic syndrome. No secondary outcomes pre-specified for child as an adult. Secondary outcomes pre-specified for health service use include: Number of antenatal visits or admissions, admission to neonatal intensive care unit/nursery, length of stay in neonatal intensive care unit or special care baby unit, length of postnatal stay (maternal), length of postnatal stay (baby), cost of maternal care, cost of neonatal/child/adult care.
Rao 2017 Fetal biometry for guiding the medical management of women with gestational diabetes mellitus for improving maternal and perinatal health	Rao U, de Vries B, Ross GP, Gordon A. Fetal biometry for guiding the medical management of women with gestational diabetes mellitus for improving maternal and perinatal health. Cochrane Database of	Pregnant women with singleton pregnancies who have gestational diabetes mellitus (GDM), as defined by the authors. Women with multiple pregnancy are	Comparing the use of medical therapy for GDM guided by maternal blood glucose values (glycaemic targets) only with medical therapy guided by fetal biometry on	All overview primary outcomes for maternal and neonatal outcomes pre-specified, except neurosensory disability in later childhood (as defined in reviews) for neonatal outcomes pre-specified (listed as a pre-specified secondary outcome).

Protocol ID and title registrations	Reference	Inclusion criteria for types of participants	Comparison interventions	Overview outcomes pre-specified in the protocols
(Protocol)	Systematic Reviews 2017, Issue 2. Art. No.: CD012544. DOI: 10.1002/14651858.CD012544	excluded. Data from studies including women with single and multiple pregnancies will only be extracted and analysed for women with single pregnancy and where this is not possible the study will be only included if more than 95% of the participants have a singleton pregnancy.	ultrasound, MRI or other imaging methods as well as maternal glycaemic targets. Where diet and exercise modifications are used, they should be consistent across the groups.	All overview secondary outcomes for maternal, maternal long-term (except: development of type 2 diabetes), fetal/neonatal, later infant/childhood, child as an adult and health services use pre-specified (except: length of stay in neonatal intensive care unit or special care baby unit).
Dunn 2016 Planned elective birth for pregnant women with gestational diabetes (Title registration)	Dunne F, Biesty LM, Egan A, Devane D, Dempsey E, Meskell P, Smith V.	Awaiting protocol publication	Awaiting protocol publication	Awaiting protocol publication
Okesene-Gafa 2016 Probiotics for treating women with gestational diabetes for improving maternal and fetal health and well-being (Title registration)	Okesene-Gafa KAM, Brown J, Crowther CA, McCowan L.	Awaiting protocol publication	Awaiting protocol publication	Awaiting protocol publication
Wang 2016 Chinese herbal medicines for treating gestational diabetes mellitus (Title registration)	Wang CC, Li L, Li R, Tam WH, Dou L.	Awaiting protocol publication	Awaiting protocol publication	Awaiting protocol publication

Table 2.5: Characteristics of included Cochrane systematic reviews

Review ID and title	Date of Search and date assessed as up to date	No. included trials (countries, design and publication years)	No. of participants in included trials	Inclusion and exclusion criteria for types of participants	Interventions and Comparisons
Boulvain 2001 Elective delivery in diabetic pregnant women	Search: 24.07.09 Up-to-date: 05.07.04 *Not up-to-date*	Trials: 1 RCT Country: USA Published: 1993: 1 RCT	200 women 200 babies no children	Women diagnosed with pre-gestational or gestational diabetes, treated with insulin or diet alone. Exclusion criteria not described.	Comparing any dietary advice with each other; comparing two or more forms of the same type of dietary advice with each other and/or different intensities of dietary interventions with each other.
Brown 2017a Oral anti-diabetic pharmacological therapies for the treatment of women with gestational diabetes.	Search: 16.05.16 (databases); 14.05.16 (clinical trial registries) Up-to-date: 14.05.16 *Up-to-date*	Trials: 11 RCTs Country: Brazil (3 RCTs); India (2 RCTs); Israel (1 RCT); UK (1 RCT); South Africa (1 RCT); USA (3 RCTs) Published: 1971: 1 RCT 2005: 1 RCT 2006: 1 RCT 2010: 1 RCT 2012: 1 RCT 2014: 1 RCT 2015: 5 RCT	1487 women 1487 babies no children	Women diagnosed with GDM (diagnosis as defined by the individual trial). Women with type 1 or type 2 diabetes diagnosed prior to pregnancy were excluded.	Comparing oral pharmacological anti-diabetic agents used during pregnancy (including metformin, glibenclamide, acarbose, tolbutamide, chlorpropamide or combination of these therapies) with either placebo or no pharmacological treatment or one agent versus another agent or versus another intervention but not insulin.
Brown 2017b Lifestyle interventions for the treatment of women with gestational diabetes	Search: 14.05.16 Up-to-date: 14.05.16 *Up-to-date*	Trials: 15 RCTs Country: Australia (1 RCTs); Canada (1 RCT); China (2 RCTs); Italy (1 RCT); Iran (2 RCTs); Thailand (1 RCT); UK (1 RCT); United Arab Emirates (1 RCT); USA (4 RCTs); multicentre (Australia and UK, 1 RCT) Published: 1989: 1 RCT 1997: 1 RCT 2000: 1 RCT 2003: 1 RCT 2004: 1 RCT 2005: 1 RCT	4501 women 3768 babies 767 children	Women diagnosed with GDM (diagnosis as defined by the individual trial). Women with known type 1 or type 2 diabetes were excluded.	Comparing lifestyle interventions (a combination of at least two or more, including standard dietary advice, with or without adjunctive pharmacotherapy (oral anti-diabetic pharmacological therapies or insulin)) versus standard care, expectant management or another lifestyle interventions or combination of lifestyle interventions. Intensive intervention were defined in included reviews as: standard dietary advice, glucose monitoring five days a week, HbA1c monthly, serial ultrasound, Doppler studies, cardiotocography (CTG monitoring) compared with usual care (dietary advice, HbA1c monthly); or individualised-dietary advice, advice on self-monitoring of blood glucose) compared with

Review ID and title	Date of Search and date assessed as up to date	No. included trials (countries, design and publication years)	No. of participants in included trials	Inclusion and exclusion criteria for types of participants	Interventions and Comparisons
		2008: 2 RCTs 2009: 1 RCT 2011: 1 RCT 2014: 5 RCTs			usual care; or structured pharmaceutical care, structured education, self-monitoring of blood glucose compared with usual care (no additional education or pharmacist counselling); or individualised advice on diet, exercise and breastfeeding compared with usual care (printed material only in prenatal and postnatal period; or dietary counselling, self-glucose monitoring, bi-weekly review, monitoring of fetal growth, amniotic volume and cardiac size compared with usual care (no dietary counselling); or diet and exercise advice, self-monitoring of blood glucose, insulin if required, fortnightly specialist review) versus usual care (no details). Other interventions used were: Group session on education and diet followed by specific dietary advice compared with group session on education and diet followed by standard clinical care and advice; or diet alone compared with diet plus supervised exercise; or relaxation training (education, breathing, muscle relaxation, mental imagery, and contacted by telephone by the researcher three times per week) compared with usual care (no details); or nutritional counselling and diet therapy +/- insulin plus self-monitoring of blood glucose compared with usual care +/- insulin plus self-monitoring of blood glucose; or intensive education and spiritual intervention compared with standard education; or face-to-face education (risks of GDM, training on glycaemic control, exercise, diet, medication and follow-up) compared with usual care (no details); or individualised and group dietary and physical activity counselling, self-monitoring blood glucose compared with usual care (group education on exercise and physical activity, not specifically taught blood

Review ID and title	Date of Search and date assessed as up to date	No. included trials (countries, design and publication years)	No. of participants in included trials	Inclusion and exclusion criteria for types of participants	Interventions and Comparisons
					glucose self-monitoring); or mindfulness eating and yoga compared with standard diabetes care (no details); or combined behavioural and exercise compared with individualised-dietary advice alone.
Brown 2017c Exercise for pregnant women with gestational diabetes for improving maternal and fetal outcomes	Search: 27.08.16 (and 18.08.16 for trial registries) Up-to-date: 18.08.16 *Up-to-date*	Trials: 11 RCTs Countries: USA (3 RCTs); Brazil (3 RCTs); Canada (2 RCTs); Italy (1 RCT); Australia(1RCT); Thailand (1 RCT) Published: 1989: 1 RCT; 1991: 1 RCT; 1997: 1 RCT; 2004: 1 RCT; 2010: 1 RCT; 2012: 1 RCT; 2014: 4 RCTs; 2015: 1 RCT	638 women 638 babies no children	Pregnant women diagnosed with GDM (as defined by trialists). Women with known pre-gestational diabetes (type 1 or type 2 diabetes) were excluded.	Comparing any type of exercise programme (+/- standard care) at any stage of pregnancy versus standard care or another intervention. Exercises summarised from reviews included individualised exercises follow-up by kinesiologist; timed exercises 2 - 4 times weekly with or without supervision and telephone counselling; brisk walking or resistance exercises: 30 minutes circuit workout with elastic-band exercises; exercises in lab conditions on cycles; home-based exercises; supervised arm ergometer training plus diet; low-intensity aerobic training in cycle-ergometer and mindfulness eating and yoga exercise.
Brown 2016a Dietary supplementation with myo-inositol in women during pregnancy for treating gestational diabetes.	Search: 14.05.16 Up-to-date: 14.05.16 *Up-to-date*	Trials: 2 RCTs Country: Italy (2 RCTs) Published: 2011: 1 RCT 2013: 1 RCT	159 women 159 babies no children	Pregnant women with a diagnosis of GDM (as defined by trialists). Women with pre-existing type 1 or type 2 diabetes were excluded.	Comparing any dose of myo-inositol, alone or in a combination preparation for the treatment of women with GDM with women who received no treatment, placebo or another intervention. The two included trials assessed 4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice.
Han 2017 Different types of dietary advice for women with gestational diabetes mellitus.	Search: 08.03.16 Up-to-date: 22.03.16 *Up-to-date*	Trials: 19 RCTs Countries: Australia (3 RCTs), Canada (2 RCTs), China (2 RCTs), Denmark (1 RCT), Italy (2 RCTs); Iran (4 RCTs); Mexico (1 RCT); Poland (1	1398 women 1398 babies no children	Women with GDM regardless of gestation, age, parity or plurality. Exclusion criteria not described.	Comparing any dietary advice with each other; comparing two or more forms of the same type of dietary advice with each other and/or different intensities of dietary interventions with each other. These trials include: low-moderate GI diet versus moderate-high GI diet, energy-restricted

Review ID and title	Date of Search and date assessed as up to date	No. included trials (countries, design and publication years)	No. of participants in included trials	Inclusion and exclusion criteria for types of participants	Interventions and Comparisons
		RCT); Spain (1 RCT); USA (2 RCT) Published: 1990: 1 RCT 1995: 1 RCT 1997: 1 RCT 2000: 1 RCT 2001: 1 RCT 2007: 1 RCT 2009: 1 RCT 2010: 1 RCT 2011: 2 RCTs 2012: 1 RCT 2013: 3 RCTs 2014: 2 RCTs 2015: 3 RCTs			diet versus no energy-restricted diet, DASH (Dietary Approaches to Stop Hypertension) diet versus control diet with matching macronutrient contents, low-carbohydrate diet versus high-carbohydrate diet, high unsaturated fat diet versus low unsaturated diet with matching calories, low-GI diet versus high-fibre moderate-GI diet, diet recommendation and diet-related behavioural advice versus diet recommendation, soy protein-enriched diet versus no soy protein diet, high-fibre versus standard-fibre diet, ethnic-specific diet versus standard healthy diet.
Han 2012 Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria.	Search: 30.09.11 Up-to-date: 21.11.11 *Not up-to-date*	Trials: 4 RCTs Country: Canada (1 RCT); Italy (1 RCT); USA (2 RCTs) Published: 1989: 1 RCT 1999: 1 RCT 2005: 1 RCT 2011: 1 RCT	543 women 543 babies no children	Pregnant women with hyperglycaemia, regardless of gestation, age, parity or plurality, who do not meet the diagnostic criteria for GDM based on OGTT results defined by trialists. Women with pre-existing diabetes mellitus and previously treated GDM were not eligible.	Comparing any form of management for women with pregnancy hyperglycaemia not meeting GDM criteria with standard antenatal care, included any type of dietary advice (standard or individualised), exercise and lifestyle advice (standard or individualised) and drug treatment including insulin and oral drugs with one type of intervention compared with standard antenatal care.
Martis 2016a Different intensities of glycaemic control for women with gestational diabetes mellitus.	Search: 31.01.16 Up-to-date: 31.01.16 *Up-to-date*	Trials: 1 RCT Country: Canada Published: 1998: 1 RCT	180 women 180 babies no children	All pregnant women diagnosed with GDM (screening and subsequent diagnosis and diagnostic criteria as identified in the individual trials). Women with known pre-existing type 1 or type 2 diabetes are excluded.	Comparing any glycaemic treatment targets used to guide treatment for women with GDM with another glycaemic target. Strict intensity of glycaemic control is defined in this one trial as: pre-prandial 5.0 mmol/L (90 mg/dL) and at one-hour postprandial: 6.7 mmol/L (120 mg/dL). Less strict glycaemic control is defined as: pre-prandial 5.8 mmol/L (104 mg/dL) and at one-hour postprandial 7.8 mmol/L (140 mg/dL).

RCT: Randomised Controlled Trial

Description of included reviews

Population -

Table 2.5 provides details of the characteristics of the included reviews including details of the inclusion and exclusion criteria of the participants. All of the included reviews included trials that recruited women with GDM.

Settings -

Table 2.5 provides details of the characteristics of the included reviews including details of the settings of the trials. There is a lack of trials from lower- and middle- income countries.

Interventions and comparisons

Of the eight Cochrane systematic reviews included (Table 2.5):

- One review focused on any dietary modifications for women with GDM:
    - Different types of dietary advice for women with gestational diabetes mellitus (Han 2017)
- One review focused on any exercise for women with GDM:
    - Exercise for pregnant women with gestational diabetes for improving maternal and fetal outcomes (Brown 2017c)
- One review focused oral pharmacological interventions for treatment for women with GDM:
    - Oral anti-diabetic pharmacological therapies for the treatment of women with gestational diabetes (Brown 2017a)
- One review assessed nutraceuticals or other dietary supplements for treatment for women with GDM:
    - Dietary supplementation with myo-inositol in women during pregnancy for treating gestational diabetes (Brown 2016a)
- Two reviews assessed other management strategies for women with GDM:

- Elective delivery in diabetic pregnant women (Boulvain 2001). The results of this review are for women diagnosed with pre-gestational diabetes or GDM. The data could not be separated out for the two different groups. The overview review authors agreed to include this review as the results were based on 187 (93.5 %) women with GDM and 13 (6.5 %) women with pre-gestational diabetes (defined as type 1 and type 2 diabetes). Furthermore, during email correspondence with the review author, it was confirmed that future up-dates of the review will separate the results for women with GDM and women with pre-gestational diabetes.
- Different intensities of glycaemic control for women with gestational diabetes mellitus (Martis 2016a)

- One review assessed interventions for women with hyperglycaemia not meeting gestational diabetes and type 2 diagnostic criteria

  - Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diagnostic criteria (Han 2012). The overview review authors agreed to include Han's 2012 review into this overview, as different countries have different diagnostic levels for confirming that a pregnant woman has GDM. It is highly possible that women with hyperglycaemia identified in one country as not meeting the gestational diagnostic threshold for GDM would be diagnosed as having GDM in another country.

- One review assessed lifestyle interventions for women with GDM

  - Lifestyle interventions for the treatment of women with GDM (Brown 2017b). Lifestyle interventions include at least two or more interventions such as dietary advice, self-monitoring blood glucose monitoring, education via group sessions or individual, mindfulness eating, yoga, relaxation, breathing, fetal growth monitoring and other antenatal tests.

In total there were 62 RCTs in these eight Cochrane systematic reviews involving a total 9133 women, 8373 babies and 767 children (Table 2.5). The eight reviews included between one RCT (Boulvain 2001; Martis 2016a) to 19 RCTs (Han 2017); and between 159 (Brown 2016a) to 4501 Brown 2017b women, with 159 (Brown 2016a) to 3768 babies (Brown 2017b); and data were reported for 767 children in one review (Brown 2017b).

Six (75 %) of the included reviews had conducted searches in the last two years and were considered up-to-date (January 2016 - August 2016) (Brown 2017a; Brown 2017b; Brown 2017c; Brown 2016a;

Han 2017; Martis 2016a). The other two reviews had their last search date listed as 24.07.09 (Boulvain 2001) and 30.09.11 (Han 2012) (Table 2.5).

Table 2.5: *Characteristics of included reviews* describes the inclusion and exclusion criteria for the types of participants for each review and its intervention and comparison.

Outcomes reported

We listed the pre-specified overview outcomes and identified whether the included systematic review had included these outcomes or not (Table 2.6).

Table 2.6: Pre-specified overview outcomes in included reviews

Included Review Author and Year →	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
Overview Primary Outcomes								
Maternal								
Hypertensive disorders of pregnancy (including preeclampsia, pregnancy-induced hypertension, eclampsia as defined in reviews)	x	√	√	√	√	√	√ secondary outcome and pre-eclampsia only in this review	√
Mode of birth (caesarean section)	√	√ called 'caesarean section' in the review	√	√	√ called 'caesarean section' in the review	√	√ includes also normal vaginal birth and operative vaginal birth	√ secondary outcome called 'caesarean section' in the review
Development of type 2 diabetes	x	√	√	√	√	√	x	√
Neonatal								
Perinatal (fetal and neonatal death) and later infant mortality	√	√	√	√ does not include later infant mortality	√ called 'perinatal mortality (stillbirth and neonatal mortality)' in review; does not include later infant mortality	√ does not include later infant mortality	√ does not include later infant mortality	√ later infant mortality not stated
Large-for-gestational age (as defined in reviews)	x	√	√	√	√	√	√	√

Included Review Author and Year →	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
Death or serious morbidity composite (as defined in reviews, e.g. perinatal or infant death, shoulder dystocia, bone fracture or nerve palsy)	√ called 'traumatic delivery (intracranial haemorrhage, fracture, brachial plexus injury)' in review, but does not include shoulder dystocia, listed under secondary outcomes in review	√	√	√	√	√	x	√
Neurosensory disability in later childhood (as defined in reviews)	√ 'long term disability in childhood' in this review	√	√	√	√ 'neurosensory disability' in this review	√	x	√
Overview Secondary Outcomes								
Maternal								
Use of additional pharmacotherapy	x	√	√	√	√	√	√	√
Maternal hypoglycaemia (as defined in the reviews)	x	√	√	√	√	√	x	√
Glycaemic control during/end of treatment (as defined in the reviews)	x	√	√	√	√	√	x	√
Weight gain in pregnancy	x	√	√	√	√	√	√	√
Adherence to the intervention	x	√	√	√	√	√	√	√
Induction of labour	x	√	√	√	√	√	√	√
Placental abruption	x	√	√	√	√	√	x	√
Postpartum haemorrhage (as defined in the reviews)	x	√	√	√	√	√	√	√

Included Review Author and Year →	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
Postpartum infection	x	√	√	√	√	√	√	√
Perineal trauma/tearing	√ (third and fourth degree perineal tear, any perineal trauma)' in review	√	√	√	√	√	√	√
Breastfeeding at discharge, six weeks postpartum, six months or longer	x	√	√	√	√ only states 'at discharge and six-week post-partum' in review	√	√	√ states only breastfeeding
Maternal mortality	x	√	√	√	√	√	√	√
Sense of well-being and quality of life	x	√	√	√	√	√	√	√
Behavioural changes associated with the treatment	x	√	√	√	√	√	x	√
Women's view of the intervention	√ (called 'women's view of their care)' in review	√	√	√	√	√	√	√
Relevant biomarker changes associated with the intervention (including adiponectin, free fatty acids, triglycerides, high-density lipoproteins, low-density lipoproteins, insulin)	x	√	√	√	√	x	x	√
Maternal long-term								
Postnatal depression	x	√	√	√	√	√	x	√
Body mass index (BMI)	x	√	√	√	√	√	√	√

Included Review Author and Year →	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
Postnatal weight retention or return to pre-pregnancy weight	x	√	√	√	√	√	√	√
Development of type 2 diabetes	x	√	x	√	x	√	√	x
Impaired glucose tolerance	x	√	√	√	√	√	√	√
Subsequent gestational diabetes	x	√	√	√	√	√	√	√
Cardiovascular health (as defined in the reviews including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)	x	√	√	√	√	√	x	√
Fetal/neonatal								
Stillbirth	x	√	√	√	√	√	x	√
Neonatal death	x	√	√	√	√	√	x	√
Macrosomia (>4000 g; or as defined in the reviews)	x	√	√	√	√	√	√ primary outcome; > 4000 g and > 4500 g	√
Small-for-gestational age (as defined in the reviews)	x	√	√	√	√	√	√	√

Included Review Author and Year →	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
Birth trauma (e.g. shoulder dystocia, bone fracture, nerve palsy)	√ Shoulder dystocia only	√	√	√	√ shoulder dystocia, bone fracture and nerve palsy, all separated out as secondary outcomes by themselves in this review	√ shoulder dystocia, bone fracture and nerve palsy, all separated out as outcomes by themselves in this review	√ shoulder dystocia, bone fracture and nerve palsy, all separated out as outcomes by themselves in this review	√ shoulder dystocia, bone fracture and nerve palsy, all separated out as outcomes by themselves in this review
Gestational age at birth	x	√	√	√	√	√	√	√
Preterm birth (< 37 weeks' gestation and < 32 weeks' gestation)	x	√	√	√	√	√	√	√
Five-minute Apgar < 7	√ 'low 5 minutes Apgar score, as defined by authors in the studies'	√	√	√	√	√	√	√
Birthweight and z score	x	√	√	√	√	√	√ birth weight only	√
Head circumference and z score	x	√	√	√	√	√	x	√
Length and z score	x	√	√	√	√	√	x	√
Ponderal index	x	√	√	√	√	√ at birth only	√	√
Adiposity (including skinfold thickness measurements (mm), fat mass)	x	√	√	√	√	√	√	√
Neonatal hypoglycaemia (as defined in the reviews)	√	√	√	√	√	√	√	√
Respiratory distress syndrome	x	√	√	√	√	√	√	√

Included Review Author and Year →	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
Neonatal jaundice (hyperbilirubinaemia) (as defined in the reviews)	x	√	√	√	√	√	√	√
Hypocalcaemia (as defined in the reviews)	x	√	√	√	√	√	x	√
Polycythaemia (as defined in the reviews)	x	√	√		√	√	x	√
Relevant biomarker changes associated with the treatment (including insulin, cord c-peptide)	x	√	√	√	√	x	x	√
Later infant/childhood								
Weight and z scores	x	√	√	√	√	√	√ weight only	√
Height and z scores	x	√	√	√	√	√	√ height only	√
Head circumference and z scores	x	√	√	√	√	√	x	√
Adiposity (including BMI, skinfold thickness, fat mass)	x	√	√	√	√	√	√ three separate outcomes: BMI, fat mass/fat-free mass, skinfold thickness measurements	√
Educational attainment	x	√	√	√	√	√ only education achievement	√ only education achievement	√
Blood pressure	x	√	√	√	√	√	√	√
Development of type 1 diabetes	x	√	√	√	√	√	√	√

Included Review Author and Year →	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
Development of type 2 diabetes	x	√	√	√	√	√	√	√
Impaired glucose tolerance	x	√	√	√	√	√	√	√
Dyslipidaemia or metabolic syndrome	x	√	√	√	√	√	√	√
Child as an adult								
Weight and z scores	x	√ weight only	√ weight-only	√	√ weight only	√ weight only	√ weight only	√ weight only
Height and z scores	x	√ height only	√ height only	√	√ height only	√ height only	√ height only	√ height only
Adiposity (including BMI, skinfold thickness, fat mass)	x	√	√	√	√	√	√ as three separate outcomes: BMI, fat mass/fat-free mass, skinfold thickness measurements	√
Cardiovascular health (as defined by trialists including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)	x	√	√	√	√	√	√ blood pressure only	√
Employment, education and social status/achievement	x	√	√	√	√	√	√ education achievements only	√
Dyslipidaemia or metabolic syndrome	x	√	√	x	√	√	√	√
Development of type 1 diabetes	x	√	√	√	√	√	√	√

Included Review Author and Year →	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
Development of type 2 diabetes	x	√	√	√	√	√	√	√
Impaired glucose tolerance	x	√	√	√	√	√	√	√
Health service use								
Number of antenatal visits or admissions	x	√	√	√	√	√	√ visits only, not admissions	√
Number of hospital or health professional visits (including midwife, obstetrician, physician, dietician, diabetic nurse)	x	√	√	√	√	√	√ dietician and medical physician visits only but each a separate outcome	√
Admission to neonatal intensive care unit/nursery	√	√	√	√	√	√	√	√
Length of stay in neonatal intensive care unit or special care baby unit	x	√	√	√ called 'duration'	x	x	x	x
Length of antenatal stay	x	√	√	√ called 'duration of maternal and neonatal hospital stay (antenatal, neonatal, postnatal)'	√	√	x	√
Length of postnatal stay (maternal)	x	√	√	√ called 'duration of maternal and neonatal hospital stay (antenatal, neonatal, postnatal)'	√	√	√	√

Included Review Author and Year →	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
Length of postnatal stay (baby)	x	√	√	√ called 'duration of maternal and neonatal hospital stay (antenatal, neonatal, postnatal)'	√	√	√	√
Cost of maternal care	x	√	√	√	√	√	√	√
Cost of neonatal/child/adult care	x	√ called 'cost of offspring care in this review'	√ called 'cost of offspring care in this review'	√ called 'cost of offspring care in this review'	√ called 'cost of offspring care in this review'	√ called 'cost of offspring care in this review'	√ called 'cost of offspring care in this review'	√ called 'cost of offspring care in this review'
Costs associated with the treatment	x	√ called 'costs associated with the intervention'	√	√ called 'costs associated with the intervention'	√	√	√ only 'costs for blood glucose monitoring during pregnancy'	√
Costs to families associated with the treatment (e.g. change of diet, extra antenatal visits, etc)	x	√ called 'costs to families associated with the management provided'	√	√	√	√	√	√

√ = pre-specified overview review outcome included in Cochrane systematic review **x** = pre-specified overview review outcome NOT included in Cochrane systematic review

Description of excluded reviews

We excluded 7 systematic reviews. Two reviews had been withdrawn as they were superseded (Walkinshaw 1996; Walkinshaw 2006); one review (Alwan 2009) has been split into three new titles, of which two have been published as reviews (Brown 2017a; Brown 2017b;) and another review (Ceysens 2006) was not up-to-date and has been superseded with a new title and is now published as a review entitled 'Exercise for pregnant women with gestational diabetes for improving maternal and fetal outcomes' (Brown 2017c). Three reviews did not include GDM as an outcome (Vitamin D - DeRegil 2016; Vitamin A - McCauley 2015; Vitamin C - Rumbold 2015) (Table 2.2).

Methodological quality of included reviews

Cochrane risk of bias assessments from included reviews

All of the included reviews stated that the overall judgement for risk of bias for the trials included in their reviews was unclear due to lack of reporting of methodological details. Specific details of the assessment of risk of bias reported in the included reviews is summarised in Table 2.7.

Table 2.7: Cochrane risk of bias assessments from included reviews

Review ID and title	Summary of trial limitations (risk of bias)	Overall risk of bias
Boulvain 2001 Elective delivery in diabetic pregnant women	**Sequence generation:** not reported **Allocation concealment:** 1 RCT unclear risk **Blinding (participants and personnel):** not reported **Blinding (outcome assessors):** not reported **Incomplete outcome data:** not reported **Selective reporting:** not reported **Other:** not reported	"The method of randomizations and of concealment of the allocation was not reported" - unclear risk of bias
Brown 2017a Oral anti-diabetic pharmacological therapies for the treatment of women with GDM	**Sequence generation:** 5 RCTs low risk; 6 unclear risk **Allocation concealment:** 6 RCTs low risk; 5 RCTs unclear risk **Blinding (participants and personnel):** 2 RCTs low risk; 7 RCTs high risk; 2 RCTs unclear risk **Blinding (outcome assessors):** 2 RCTs low risk; 9 RCTs unclear risk **Incomplete outcome data:** 7 RCT low risk; 2 RCTs high risk; 2 RCTs unclear risk **Selective reporting:** 3 RCTs low risk; 8 RCTs high risk **Other:** 3 RCT's low risk; 6 RCTs high risk; 2 RCTs unclear risk	"The overall risk of bias was 'unclear' due to inadequate reporting of methodology"
Brown 2017b Lifestyle interventions for the treatment of women with GDM	**Sequence generation:** 10 RCTs low risk; 5 RCTs unclear risk **Allocation concealment:** 5 RCTs low risk; 10 RCTs unclear risk **Blinding (participants and personnel):** 9 RCTs high risk; 4 RCTs low risk; 2 RCTs unclear risk **Blinding (outcome assessors):** 6 RCTs low risk; 9 RCTs unclear risk **Incomplete outcome data:** 3 RCTs high risk; 10 RCTs low risk; 2 RCTs unclear risk **Selective reporting:** 11 RCTs high risk; 3 RCTs low risk; 1 RCT unclear risk **Other:** 2 RCTs high risk; 13 RCTs low risk	"Overall the evidence was judged to be of unclear risk of bias due to inadequate reporting of allocation concealment and blinding of outcome assessors and selective outcome reporting. There is variation between the trials with regards to the content of the lifestyle interventions. The evidence is dominated by two large trials (Crowther 2005; Landon 2009) that included 1000 women and 958 women, respectively. Both of these trials were judged to be at low risk of bias"
Brown 2017c Exercise for pregnant women with GDM for improving maternal and fetal outcomes	**Sequence generation:** 4 RCTs low risk; 7 RCTs unclear risk **Allocation concealment:** 3 RCTs low risk; 8 RCTs unclear risk **Blinding (participants and personnel):** 3 RCTs high risk; 8 RCTs unclear risk **Blinding (outcome assessors):** 2 RCTs low risk; 9 RCTs unclear risk **Incomplete outcome data:** 2 RCTs high risk; 3 RCTs low risk; 6 RCTs unclear risk **Selective reporting:** 1 RCT low risk; 10 RCTs unclear risk **Other:** 3 RCTs low risk; 8 RCTs unclear risk	"We judged the overall risk of bias of the included studies to be unclear due to lack of methodological details"

Review ID and title	Summary of trial limitations (risk of bias)	Overall risk of bias
Brown 2016a Dietary supplementation with myo-inositol in women during pregnancy for treating GDM	**Sequence generation:** 2 RCTs low risk **Allocation concealment:** 1 RCT low risk; 1 RCT unclear risk **Blinding (participants and personnel):** 1 RCT low risk; 1 RCT unclear risk **Blinding (outcome assessors):** 2 RCTs unclear risk **Incomplete outcome data:** 1 RCT low risk; 1 RCT unclear risk **Selective reporting:** 1 RCT high risk; 1 RCT unclear risk **Other:** 2 RCT's low risk	"Overall, the risk of bias of the included studies was judged to be unclear due to the lack of key methodological information"
Han 2017 Different types of dietary advice for women with GDM	**Sequence generation:** 11 RCTs low risk; 8 RCTs unclear risk **Allocation concealment:** 4 RCTs low risk; 14 RCTs unclear risk; 1 RCT high risk **Blinding (participants and personnel):** 4 RCTs low risk; 2 RCTs unclear risk; 13 RCTs high risk **Blinding (outcome assessors):** 2 RCTs low risk, 16 RCTs unclear risk; 1 RCT high risk **Incomplete outcome data:** 14 RCTs low risk; 3 RCTs unclear risk; 2 RCTs high risk **Selective reporting:** 16 RCTs unclear risk; 3 RCTs high risk Other: 2 RCT's low risk	"In this update, we included 19 trials randomising 1398 women with GDM, at an overall unclear to moderate risk of bias"
Han 2012 Interventions for pregnant women with hyperglycaemia not meeting GDM and type 2 diabetes diagnostic criteria	**Sequence generation:** 4 RCTs unclear risk **Allocation concealment:** 1 RCT low risk; 3 RCTs unclear risk **Blinding (participants and personnel):** 4 RCTs high risk **Blinding (outcome assessors):** 4 RCTs unclear risk **Incomplete outcome data:** 2 RCTs low risk; 2 RCTs high risk **Selective reporting:** 3 RCTs low risk; 1 RCT high risk **Other:** 4 RCTs low risk	"Three included studies were at moderate to high risk of bias and one study was at low to moderate risk of bias"
Martis 2016a Different intensities of glycaemic control for women with GDM	**Sequence generation**: 1 RCT unclear risk **Allocation concealment:** 1 RCT unclear risk **Blinding (participants and personnel):** 1 RCT high risk **Blinding (outcome assessors):** 1 RCT unclear risk **Incomplete outcome data:** 1 RCT unclear risk **Selective reporting:** 1 RCT high risk **Other:** 1 RCT high risk	"The overall quality of the included trial was judged to be unclear as conference abstract only"

GRADE Assessment

The quality of the evidence reported for the eight included reviews as assessed by the Cochrane systematic review authors using the GRADE method varied widely ranging from very low- to high-quality, with the majority of studies being assessed as low- to very low-quality. See Table 2.8; Table 2.9; Table 2.10 for details on the following pages.

The quality of the evidence reported additionally for *all* overview review secondary outcomes using the four GRADE quality ratings varied widely ranging from very low- to high-quality. See Table 2.11; Table 2.12; Table 2.13; Table 2.14; Table 2.15 for details on the following pages.

Table 2.8: GRADE Summary of findings table - Maternal

Intervention and comparison	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks Comments without quotation marks from overview review authors
1.0 Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia, as defined in reviews)						
Brown 2017a Oral anti-diabetic agents versus placebo (Glibenclamide versus placebo) **Any hypertensive disorders of pregnancy, not defined**	167 per 1000	**207 per 1000** (135 to 317)	**RR 1.24** (0.81 to 1.90)	375 (1 RCT)	Very low	"Evidence is based on one study and 93% were Hispanic women, results may not be generalisable to other populations. There is risk of bias, as we did not find a published protocol and there were more outcomes reported in the published paper than were listed in the trial registration document".
Brown 2017a Metformin versus glibenclamide **Any hypertensive disorders of pregnancy, not defined**	88 per 1000	**62 per 1000** (33 to 114)	**RR 0.70** (0.38 to 1.30)	508 (3 RCTs)	Moderate	"All studies were open label, some risk of bias".
Brown 2017a Oral anti-diabetic agents versus placebo (Glibenclamide versus placebo) **Pregnancy induced hypertension**	102 per 1000	**127 per 1000** (73 to 224)	**RR 1.24** (0.71 to 2.19)	375 (1 RCT)	Low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect.
Brown 2017a Metformin versus Glibenclamide **Pregnancy induced hypertension**	108 per 1000	**77 per 1000** (40 to 148)	**RR 0.71** (0.37 to 1.37)	359 (2 RCT)	Moderate	Risk of performance bias as study participants and care providers were not blinded in both trials and additionally one trial had reporting bias for not reporting pre-specified outcome for macrosomia.
Han 2017 Low carbohydrate diet versus high-carbohydrate diet **Pregnancy induced hypertension**	133 per 1000	**53 per 1000** (17 to 163)	**RR 0.40** (0.13 to 1.22)	150 (1 RCT)	Very low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect. Risk of performance bias as study participants and care providers were not blinded.

Intervention and comparison	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks Comments without quotation marks from overview review authors
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **Pregnancy induced hypertension**	143 per 1000	**77 per 1000** (9 to 751)	**RR 0.54** (0.06 to 5.26)	27 (1 RCT)	Very low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect. Risk of performance bias as study participants and care providers were not blinded.
Han 2017 Ethnic specific diet versus standard healthy diet **Pregnancy induced hypertension**	100 per 1000	**33 per 1000** (2 to 732)	**RR 0.33** (0.02 to 7.32)	20 (1 RCT)	Very low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect. Risk of performance bias as study participants and care providers were not blinded and reporting bias as outcomes were reported in figures with no variance measures and no access to the study protocol.
Brown 2017a Oral anti-diabetic agents versus placebo (Glibenclamide versus placebo) **Severe hypertension or pre-eclampsia**	65 per 1000	**79 per 1000** (38 to 165)	**RR 1.23** (0.59 to 2.56)	375 (1 RCT)	Low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect.
Han 2017 Low-moderate GI diet versus moderate-high GI diet **Severe hypertension or pre-eclampsia**	21 per 1000	**21 per 1000** (2 to 333)	**RR 1.02** (0.07 to 15.86)	95 (1 RCT)	Very low	"Evidence is based on one study in China. Study results may not be generalisable to other populations. Imprecision as wide confidence interval crossing the line of no effect with few events and small sample size".
Brown 2017a Metformin versus Glibenclamide **Pre-eclampsia**	41 per 1000	**27 per 1000** (4 to 155)	**RR 0.66** (0.11 to 3.82)	149 (1 RCT)	Very low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect. Study participants and care providers were not blinded.
Han 2017 Energy restricted diet versus no energy-restricted diet **Pre-eclampsia**	222 per 1000	**222 per 1000** (113 to 437)	**RR 1.00** (0.51 to 1.97)	117 (1 RCT)	Low	"Evidence is based on one study. Imprecision as wide confidence interval crossing the line of no effect and small sample size".

Intervention and comparison	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks Comments without quotation marks from overview review authors
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents **Pre-eclampsia**	74 per 1000	**74 per 1000** (0.31 to 240)	**RR 1.00** (0.31 to 3.26)	136 (3 RCTs)	Moderate	Imprecision as wide confidence interval crossing the line of no effect.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **Pre-eclampsia**	0 per 1000	**0 per 1000** (0 to 0)	RR not estimable	27 (1 RCT)	Low	Evidence is based on one study. Risk of performance bias as study participants and care providers were not blinded. Further risk of bias as both groups of participants were unbalanced for BMI at baseline. There were no events in both groups.
Han 2017 Soy protein-enriched diet versus no soy protein diet **Pre-eclampsia**	29 per 1000	**59 per 1000** (6 to 619)	**RR 2.00** (0.19 to 21.03)	68 (1 RCT)	Very low	Evidence is based on one study. Imprecision as wide confidence interval crossing the line of no effect. Risk of performance bias, as participants and personnel were not blinded.
Brown 2017b Lifestyle intervention versus usual care or diet alone **Pre-eclampsia**	129 per 1000	**90 per 1000** (51 to 157)	**RR 0.70** (0.40 to 1.22)	2796 (4 RCTs)	Low	"Evidence of inconsistency with $I^2 > 70\%$ downgraded two levels".
Brown 2017c Exercise versus control **Pre-eclampsia**	43 per 1000	**13 per 1000** (0 to 308)	**RR 0.31** (0.01 to 7.09)	48 (2 RCTs)	Low	"Wide confidence intervals crossing the line of no effect and low event rates with a small sample size are suggestive of imprecision and lack of clarity for most items related to risk of bias".
Han 2012 Intensive management versus routine care **Pre-eclampsia**	21 per 1000	**57 per 1000** (5 to 619)	**RR 2.74** (0.26 to 29.07)	83 (1 RCT)	Low	Evidence is based on one small study with few events and serious design limitations and imprecision with wide confidence intervals crossing the line of no effect.
Han 2017 Low-moderate GI diet versus moderate-high GI diet **Eclampsia**	24 per 1000	**8 per 1000** (0 - 195)	**RR 0.34** (0.01 to 8.14)	83 (1 RCT)	Very low	"Evidence is based on one study in China. Study results may not be generalisable to other populations. Imprecision as wide confidence interval crossing the line of no effect with few events and small sample size.

Intervention and comparison	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks Comments without quotation marks from overview review authors
2.0 Caesarean section						
Boulvain 2001 Induction of labour versus expectant management	310 per 1000	**251 per 1000** (161 to 391)	**RR 0.81** (0.52 to 1.26)	200 (1 RCT)	Low	Evidence is based on one study with design limitations and imprecision with wide confidence intervals crossing the line of no effect.
Brown 2017a Oral anti-diabetic agents versus placebo (Glibenclamide versus placebo)	360 per 1000	**371 per 1000** (285 to 483)	**RR 1.03** (0.79 to 1.34)	375 (1 RCT)	Very low	"Evidence is based on one study and 93% were Hispanic women, results may not be generalisable to other populations. There is risk of bias, as we did not find a published protocol and there were more outcomes reported in the published paper than were listed in the trial registration document".
Brown 2017a Metformin versus glibenclamide	392 per 1000	**470 per 1000** (325 to 674)	**RR 1.20** (0.83 to 1.72)	554 (4 RCTs)	Low	"Three of the four studies were open label and three of four studies were unclear for blinding of outcome assessors. Two studies reported additional outcomes that were not pre-specified, and heterogeneity was high".
Brown 2017a Glibenclamide versus acarbose	526 per 1000	**500 per 1000** (279 to 895)	**RR 0.95** (0.53, 1.70)	43 (1 RCT)	Low	"Evidence is based on one study. Method of randomisation was unclear, and the study was open-label".
Han 2017 Low-moderate GI diet versus moderate-high GI diet	344 per 1000	**277 per 1000** (100 to 506)	**RR 0.66** (0.29 to 1.47)	63 (1 RCT)	Low	"Evidence is based on one study with unclear risk of selection and detection bias and high risk of performance bias. Imprecision as wide confidence interval crossing the line of no effect and small sample size".
Han 2017 Energy restricted diet versus no energy restricted diet	228 per 100	**255 per 1000** (182 to 356)	**RR 1.12** (0.80 to 1.56)	420 (2 RCTs)	Low	"Design limitations: two studies at unclear risk of selection bias; one study at high risk of performance bias and unclear risk of detection bias. Imprecision with wide confidence intervals crossing the line of no effect".
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents	837 per 1000	**444 per 1000** (310 to 636)	**RR 0.53** (0.37 to 0.76)	86 (2 RCTs)	Moderate	Unclear risk of bias for allocation concealment and selective reporting in both trials and additionally in one trial risk of bias for blinding of participants, personnel and outcome assessors.
Han 2017 Low carbohydrate diet versus high-carbohydrate diet	278 per 1000	**358 per 1000** (233 to 553)	**RR 1.29** (0.84 to 1.99)	179 (2 RCTs)	Low	Risk of performance bias as study participants and care providers were not blinded. Additionally, one study had a high risk of bias for selective reporting as limited data was reported and no access to study protocol.

Intervention and comparison	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks Comments without quotation marks from overview review authors
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories	71 per 1000	**77 per 1000** (5 to 1000)	**RR 1.08** (0.07 to 15.50)	179 (2 RCTs)	Very low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect. Risk of performance bias as study participants and care providers were not blinded. Further risk of bias as both groups of participants were unbalanced for BMI at baseline.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet	178 per 1000	**340 per 1000** (162 to 716)	**RR 1.91** (0.91 to 4.03	92 (1 RCT)	Very low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect. Risk of detection and attrition bias as study outcome assessors were not blinded and incomplete data reported. Baseline for blood glucose concentration were unbalanced between groups.
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only	260 per 1000	**203 per 1000** (99 to 421)	**RR 0.78** (0.38 to 1.62)	99 (1 RCT)	Low	Evidence is based on one study and risk of performance bias as study participants and care providers were not blinded.
Han 2017 Soy protein-enriched diet versus no soy protein diet	412 per 1000	**412 per 1000** (235 to 729)	**RR 1.00** (0.57 to 1.77)	68 (1 RCT)	Low	Evidence is based on one study and risk of performance bias as study participants and care providers were not blinded.
Han 2017 Ethnic specific diet versus standard healthy diet	500 per 1000	**600 per 1000** (270 to 1000)	**RR 1.20** (0.54 to 2.67)	20 (1 RCT)	Very low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect. Risk of performance bias as study participants and care providers were not blinded and reporting bias as outcomes were reported in figures with no variance measures and no access to the study protocol.
Brown 2017b Lifestyle intervention versus usual care or diet alone	380 per 1000	**342 per 1000** (296 to 399)	**RR 0.90** (0.78 to 1.05)	3545 (10 RCTs)	Low	"Evidence of selective reporting in more than half of the trials reporting this outcome and evidence of inconsistency with I^2 = > 50% but < 70%. There is some suggestion of asymmetry observed in the funnel plot".
Brown 2017c Exercise versus control	319 per 1000	**274 per 1000** (201 to 370)	**RR 0.86** (0.63 to 1.16)	316 (5 RCTs)	Moderate	"Lack of clarity for most items related to risk of bias".

Intervention and comparison	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks Comments without quotation marks from overview review authors
Han 2012 Intensive management versus routine care	249 per 1000	**232 per 1000** (169 to 316)	**RR 0.93** (0.68 to 1.27)	509 (3 RCTs)	Very low	Evidence based on three RCTs with serious/very serious design limitations and imprecision with wide confidence intervals crossing the line of no effect.
Martis 2016a Strict intensity[2] of glycaemic control versus less strict glycaemic control	244 per 1000	**330 per 1000** (203 to 532)	**RR 1.35** (0.83 to 2.18)	171 (1 RCT)	Very low	"Evidence based on one trial that was only published in conference abstract form. Lack of detail to make a judgement about random sequence generation, allocation concealment, attrition bias and reporting bias. Open label study and no details regarding blinding of outcome assessors was reported. Wide confidence intervals that cross the line of no effect".
3.0 Development of Type 2 diabetes						
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **OGTT[3] for diagnosis of type 2 diabetes at one to two weeks post-partum**	167 per 1000	**333 per 1000** (75 to 1000)	**RR 2.00** (0.45 to 8.94)	24 (1 RCT)	Very low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect. Risk of performance bias as study participants and care providers were not blinded. Further risk of bias as both groups of participants were unbalanced for BMI at baseline.
Han 2017 Low-GI diet versus high fibre moderate-GI diet **OGTT[3] for diagnosis of type 2 diabetes at three months post-partum**	80 per 1000	**61 per 1000** (9 to 401)	**RR 0.76** (0.11 to 5.01)	58 (1 RCT)	Very low	Imprecision - evidence is based on one study and wide confidence interval crossing the line of no effect. Risk of detection and attrition bias as study outcome assessors were not blinded and incomplete data reported. Baseline for blood glucose concentration were unbalanced between groups.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **OGTT[3] for diagnosis of type 2 diabetes at four to 13 months post-partum**	333 per 1000	**333 per 1000** (33 to 1000)	**RR 1.00** (0.10 to 9.61)	6 (1 RCT)	Very low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect. Risk of performance bias as study participants and care providers were not blinded. Further risk of bias as both groups of participants were unbalanced for BMI at baseline.

Intervention and comparison	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks Comments without quotation marks from overview review authors
Brown 2017b Lifestyle intervention versus usual care or diet alone **Test and time frame not defined**	83 per 1000	**81 per 1000** (45 to 146)	**RR 0.98** (0.54 to 1.76)	486 (2 RCTs)	Low	"Evidence of risk of bias with one of the two studies not blinding participants/researcher and evidence of risk of bias for attrition"
18.0. Perineal trauma						
Brown 2017a Oral anti-diabetic agents versus placebo (Glibenclamide versus placebo)	5 per 1000	**5 per 1000** (0 to 84)	**RR 0.98** (0.06 to 15.62)	375 (1 RCT)	Very low	"Evidence is based on one study and 93% were Hispanic women, results may not be generalisable to other populations. We did not find a published protocol and there were more outcomes reported in the published paper than were listed in the trial registration document". "There are wide confidence intervals crossing the line of no effect and low event rates suggestive of imprecision. Event rates were low 1/189 for anti-diabetic pharmacological therapy and 1/186 in the control (placebo) group".
Brown 2017a Metformin versus glibenclamide	6 per 1000	**11 per 1000** (1 to 81)	**RR 1.67** (0.22 to 12.52)	308 (2 RCTs)	Low	"All studies were open label and wide confidence intervals along with low event rates suggest imprecision. Low event rates (2/154 for metformin and 1/154 for glibenclamide".
Brown 2017b Lifestyle intervention versus usual care or diet alone	498 per 1000	**518 per 1000** (463 to 588)	**RR 1.04** (0.93 to 1.18)	1000 (1 RCT)	Moderate	"Imprecision - evidence is based on a single trial"
27.0. Return to pre-pregnancy weight						
Brown 2017b Lifestyle intervention versus usual care or diet alone **At six weeks post-partum**	173 per 1000	208 per 1000 (116 to 376)	**RR 1.20** (0.67 to 2.17)	189 (1 RCT)	Low	Imprecision - evidence based on one trial. Evidence of risk of bias as participants and researchers were not blinded and selective reporting. Wide confidence interval crossing the line of no effect.
Han 2017 Low-GI diet versus high fibre moderate-GI diet **At three months post-partum**	217 per 1000	**250 per 1000** (93 to 667)	**RR 1.15** (0.43 to 3.07)	555 (1 RCT)	Very low	Imprecision - evidence based on one trial. Evidence of risk of bias as participants and researchers were not blinded and attrition bias for incomplete data. Wide confidence interval crossing the line of no effect.

Intervention and comparison	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks Comments without quotation marks from overview review authors
Brown 2017b Lifestyle intervention versus usual care or diet alone **At seven months post-partum**	239 per 1000	**379 per 1000** (236 to 613)	**RR 1.59** (0.99 to 2.57)	159 (1 RCT)	Very low	Imprecision - evidence based on one trial. Evidence of risk of bias as participants and researchers were not blinded and selective reporting evident. Wide confidence interval crossing the line of no effect.
Brown 2017b Lifestyle intervention versus usual care or diet alone **At 12 months post-partum**	214 per 1000	**375 per 1000** (225 to 621)	**RR 1.75** (1.05 to 2.90)	156 (1 RCT)	Low	"Imprecision - evidence is based on a single trial. Evidence of risk of bias as unclear allocation concealment and no blinding of participants and researchers"
Brown 2017c Exercise versus control **At follow-up (timing not defined)**	The maternal BMI (follow-up) kg/m^2 was 0	**MD 0.11 higher** (-1.04 lower to 1.26 higher)	-	254 (3 RCTs)	High	
25.0 Post-natal depression						
Brown 2017b Lifestyle intervention versus usual care or diet alone	169 per 1000	**83 per 1000** (53 to 132)	**RR 0.49** (0.31 to 0.78)	573 (1 RCT	Low	"Imprecision - evidence is based on a single trial and evidence of risk of attrition bias"
14.0. Induction of labour						
Brown 2017a Oral anti-diabetic agents versus placebo (Glibenclamide versus placebo)	188 per 1000	**222 per 1000** (149 to 331)	**RR 1.18** (0.79 to 1.76)	375 (1 RCT)	Very low	"Evidence is based on one study and 93% were Hispanic women, results may not be generalisable to other populations. We did not find a published protocol and there were more outcomes reported in the published paper than were listed in the trial registration document".
Brown 2017a Metformin versus glibenclamide	613 per 1000	**496 per 1000** (374 to 655)	**RR 0.81** (0.61, 1.07)	159 (1 RCT)	Low	"Evidence is based on one study. Method of randomisation was unclear, and the study was open-label".
Han 2017 Low-moderate GI diet versus moderate-high GI diet	219 per 1000	**193 per 1000** (72 to 512)	**RR 0.88** (0.33 to 2.34)	63 (1 RCT)	Low	"One small study at unclear risk of selection and detection bias and high risk of performance bias. Wide confidence interval crossing the line of no effect".

Intervention and comparison	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks Comments without quotation marks from overview review authors
Han 2017 Energy restricted diet versus no energy restricted diet	451 per 1000	**460 per 1000** (307 to 690)	**RR 1.02** (0.68 to 1.53)	114 (1 RCT)	Low	"One small study at unclear risk of selection and detection bias and wide confidence interval crossing the line of no effect".
Brown 2017b Lifestyle intervention versus usual care or diet alone	211 per 1000	**252 per 1000** (220 to 285)	**RR 1.20** (0.99 to 1.46)	2699 (4 RCTs)	High	
Brown 2017c Exercise versus control	400 per 1000	**552 per 1000** (284 to 1000)	**RR 1.38** (0.71 to 2.68)	40 (1 RCT)	Low	"Imprecision - low event rates and small sample size. Lack of clarity for most items related to risk of bias".
Han 2012 Intensive management versus routine care	0 per 1000	**0 per 1000** (0 to 0)	**RR 17.69** (1.03 to 304.09)	83 (1 RCT)	Very low	Evidence is based on one small study with few events and serious design limitations and imprecision with wide confidence intervals crossing the line of no effect.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RCT:** randomised controlled trial; **RR:** risk ratio; **MD:** mean difference

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] DASH is an acronym for **D**ietary **A**pproaches to **S**top **H**ypertension
[2]Strict intensity of glycaemic control (stricter) defined in review as: pre-prandial 5.0 mmol/L (90 mg/dL) and one hour post-prandial 6.7 mmol/L (120 mg/dL) and less strict glycaemic control (liberal) defined in review as: pre-prandial 5.8 mmol/L (104 mg/dL) and one hour post-prandial 7.8 mmol/L (140 mg/dL)
[3]OGTT is an acronym for **O**ral **G**lucose **T**olerance **T**est

Table 2.9: GRADE Summary of findings table - Child (as neonate, child, adult)

Intervention and comparison and outcome	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks. Comments without quotation marks from overview review authors
5.0 Large-for-gestational age (LGA) (as defined in reviews)						
Boulvain 2001 Induction of labour versus expectant management **LGA defined as > 90th percentile**	230 per 1000	**99 per 1000** (51 to 200)	**RR 0.43** (0.22 to 0.87)	200 (1 RCT)	Low	Evidence is based on one small study with design limitations.
Brown 2017a Oral anti-diabetic agents versus placebo: (Glibenclamide versus placebo) **LGA defined > 90th percentile**	118 per 1000	**105 per 1000** (60 to 187)	**RR 0.89** (0.51 to 1.58)	375 (1 RCT)	Very low	"Evidence is based on one study and 93% were Hispanic women, results may not be generalisable to other populations. There is risk of bias, as we did not find a published protocol and there were more outcomes reported in the published paper than were listed in the trial registration document".
Brown 2017a Metformin versus glibenclamide **LGA defined as > 90th percentile**	193 per 1000	**129 per 1000** (46 to 354)	**RR 0.67** (0.24 to 1.83)	246 (2 RCTs)	Low	"Allocation concealment was unclear in one study and one study was open label. Inconsistent as heterogeneity was I^2= 54%, which could not be explained by the diagnostic criteria used".
Brown 2017a Glibenclamide versus acarbose **LGA defined as > 90th percentile**	105 per 1000	**251 per 1000** (57 to 1000)	**RR 2.38** (0.54 to 10.46)	43 (1 RCT)	Low	"Evidence is based on one small study with wide confidence intervals and evidence of selective reporting".
Brown 2016a Myo-inositol versus placebo[2] **LGA defined as > 90th centile**	26 per 1000	**9 per 1000** (1 to 226)	**RR 0.36** (0.02 to 8.58)	73 (1 RCT)	Low	"Evidence is based on one small study with low event rates - 0/35 events in myo-inositol group and 1/38 events in the placebo group".
Han 2017 Low-moderate GI diet versus moderate-high GI diet **LGA defined as ≥ 90th percentile for gestational age**	146 per 1000	**104 per 1000** (32 to 342)	**RR 0.71** (0.22 to 2.34)	89 (2 RCTs)	Low	"One study at unclear risk of selection bias and two studies at risk of performance bias and unclear risk of detection bias. Wide confidence intervals crossing the line of no effect and small sample size".

Intervention and comparison and outcome	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks. Comments without quotation marks from overview review authors
Han 2017 Energy restricted diet versus no energy-restricted diet **LGA defined as ≥ 90th percentile for gestational age**	246 per 1000	**288 per 1000** (160 to 522)	**RR 1.17** (0.65 to 2.12)	123 (1 RCT)	Low	"One study at unclear risk of selection and detection bias and wide confidence interval crossing the line of no effect and small sample size".
Han 2017 Low carbohydrate diet versus high-carbohydrate diet **LGA defined as ≥ 90th percentile for gestational age**	80 per 1000	**41 per 1000** (10 to 156)	**RR 0.51** (0.13 to 1.95)	149 (1 RCT)	Very low	Imprecision - evidence is based on one study and wide confidence interval crossing the line of no effect. Risk of performance bias as participants and researchers were not blinded.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **LGA defined as ≥ 90th percentile for gestational age**	571 per 1000	**309 per 1000** (120 to 783)	**RR 0.54** (0.21 to 1.37)	27 (1 RCT)	Very low	Imprecision - evidence is based on one study and wide confidence interval crossing the line of no effect. Risk of performance bias as participants and researchers were not blinded. Baseline for BMI were unbalanced between groups.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **LGA defined as ≥ 90th percentile for gestational age**	44 per 1000	**128 per 1000** (27 to 600)	**RR 2.87** (0.61 to 13.50)	92 (1 RCT)	Very low	Imprecision - evidence is based on one study and wide confidence interval crossing the line of no effect. Risk of detection bias as outcome assessors were not blinded. Incomplete data reported (attrition bias) and blood glucose concentration unbalanced at baseline.
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only **LGA defined as ≥ 90th percentile for gestational age**	140 per 1000	**102 per 1000** (35 to 300)	**RR 0.73** (0.25 to 2.14)	99 (1 RCT)	Very low	Imprecision - evidence is based on one study and wide confidence interval crossing the line of no effect. Risk of performance bias as participants and personnel were not blinded.

Intervention and comparison and outcome	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks. Comments without quotation marks from overview review authors
Han 2017 Ethnic specific diet versus standard healthy diet **LGA defined as ≥ 90th percentile for gestational age**	300 per 1000	**42 per 1000** (3 to 735)	**RR 0.14** (0.01 to 2.45)	20 (1 RCT)	Very low	Imprecision - evidence is based on one study and wide confidence interval crossing the line of no effect. Risk of performance bias as participants and personnel were not blinded and selective reporting (reporting bias). Low event rates, as there were no events in the intervention group and three events in the control group.
Brown 2017b Lifestyle intervention versus usual care or diet alone **LGA not defined**	189 per 1000	**113 per 1000** (95 to 134)	**RR 0.60** (0.50 to 0.71)	2994 (6 RCTs)	Moderate	"Several included studies had high risk of bias for lack of blinding, incomplete outcome data and selective reporting. Allocation concealment was in unclear in two of the six studies".
Han 2012 Intensive management versus routine care **LGA defined as ≥ 90th percentile for gestational age**	171 per 1000	**63 per 1000** (34 to 113)	**RR 0.37** (0.20 to 0.66)	438 (3 RCTs)	Low	Evidence based on three studies with serious/very serious design limitations.
4.0 Perinatal mortality (fetal and neonatal death) and later infant mortality						
Boulvain 2001 Induction of labour versus expectant management **Perinatal death**	0 per 1000	**0 per 1000** (0 to 0)	RR not estimable	200 (1 RCT)	Very low	Evidence is based on one small study with no events and design limitations.
Brown 2017a Metformin versus glibenclamide **Perinatal death**	6 per 1000	**5 per 1000** (0 to 83)	**RR 0.92** (0.06 to 14.55)	359 (2 RCTs)	Very low	"Open label studies with no evidence of blinding of participants or researchers. Event rates were very low. One study had no event of perinatal death in either the metformin nor the glibenclamide group. The second study had one death in each group".
Brown 2017a Glibenclamide versus acarbose **Perinatal death**	0 per 1000	**0 per 1000** (0 to 0)	RR not estimable	43 (1 RCT)	Low	"Evidence based on a single small study with wide confidence intervals. No events were reported in either group. There is evidence of selective reporting".
Han 2017 Energy restricted diet versus no energy restricted diet **Perinatal death**	0 per 1000	**0 per 1000** (0 to 0)	RR not estimable	423 (2 RCTs)	Low	"Two studies at unclear risk of selection bias. One study at high risk of performance bias and unclear risk of detection bias. There were no events in either group and relatively small sample sizes".

Intervention and comparison and outcome	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks. Comments without quotation marks from overview review authors
Han 2017 Low-carbohydrate diet versus high-carbohydrate diet **Perinatal death**	0 per 1000	**0 per 1000** (0 to 0)	RR 3.00 (0.12 to 72.49)	150 (1 RCT)	Very low	Evidence is based on one study and imprecision as wide confidence interval crossing the line of no effect. Risk of performance bias as study participants and care providers were not blinded. Low event rates (one event in the control group).
Brown 2017b Lifestyle intervention versus usual care or diet alone **Perinatal death**	5 per 1000	**0 per 1000** (0 to 9)	RR 0.09 (0.01 to 1.70)	1988 (2 RCTs)	Low	"There is evidence of imprecision with wide confidence intervals and low events rates (5 perinatal deaths in one trail's control group) and one of the two trials did not blind participants/researchers".
Brown 2017c Exercise versus control **Perinatal death**	0 per 1000	**0 per 1000** (0 to 0)	RR not estimable	19 (1 RCT)	Low	Imprecision - There are no events in either group and the sample size is only 19 infants. There is a lack of clarity for most items associated with risk of bias".
6.0 Death or serious morbidity composite (as defined in reviews)						
Brown 2017a Metformin versus glibenclamide **Defined as composite of neonatal outcomes including hypoglycaemia, hyperbilirubinaemia, macrosomia, respiratory illness, birth injury, stillbirth or neonatal death**	350 per 1000	**189 per 1000** (109 to 329)	**RR 0.54** (0.31 to 0.94)	159 (1 RCT)	Low	"Evidence is based on one small study". Risk of performance bias as participants and personnel were not blinded.
Han 2017 Ethnic specific diet versus standard healthy diet **Defined as composite of neonatal outcomes that included hypoglycaemia, neonatal asphyxia, respiratory distress syndrome (RDS), hyperbilirubinaemia and hypocalcaemia**	0 per 1000	**0 per 1000** (0 to 0)	**RR not** estimable	20 (1 RCT)	Very low	Imprecision - evidence is based on one study. Risk of performance bias as participants and personnel were not blinded and selective reporting (reporting bias). No events in either group.

Intervention and comparison and outcome	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks. Comments without quotation marks from overview review authors
Brown 2017b Lifestyle intervention versus usual care or diet alone **Defined as composite of death, shoulder dystocia, bone fracture and nerve palsy in one trial and still birth, neonatal death, hypoglycaemia, hyperbilirubinaemia, elevated cord-blood C-peptide and birth trauma in the other trial**	193 per 1000	**110 per 1000** (41 to 299)	**Average RR 0.57** (0.21 to 1.55)	1930 (2 RCTs)	Very low	"Evidence of inconsistency with I^2 > 70%. One of the two trials did not blind participants/researchers and evidence of imprecision with wide confidence intervals crossing the line of no effect".
Brown 2017c Exercise versus control **Defined as mortality and morbidity composite**	65 per 1000	**36 per 1000** (8 to 169)	**RR 0.56** (0.12 to 2.61)	169 (2 RCTs)	Moderate	Imprecision - wide confidence intervals and low event rates.
44.0 Neonatal hypoglycaemia (as defined in the reviews)						
Boulvain 2001 Induction of labour versus expectant management **Not defined**	0 per 1000	**0 per 1000** (0 to 0)	not estimable	200 (1 RCT)	Very low	Evidence is based on one small study with no events and serious design limitations and imprecision with wide confidence intervals crossing the line of no effect.
Brown 2017a Oral anti-diabetic agents versus placebo: (Glibenclamide versus placebo) **Not defined**	11 per 1000	**21 per 1000** (4 to 114)	**RR 1.97** (0.36 to 10.62)	375 (1 RCT)	Very low	"Evidence is based on one study and 93% were Hispanic women, results may not be generalisable to other populations. There is risk of bias, as we did not find a published protocol and there were more outcomes reported in the published paper than were listed in the trial registration document. Event rates were low with 4/189 for oral antidiabetic pharmacological therapy (Glibenclamide) and 2/186 for placebo group with wide confidence intervals crossing the line of no effect".
Brown 2017a Metformin versus glibenclamide **Defined as < 2.2 mmol/L (< 40mg/dL)**	48 per 1000	**41 per 1000** (20 to 84)	**RR 0.86** (0.42 to 1.77)	554 (4 RCTs)	Low	"Allocation concealment was unclear in one study and one other study was open label. Event rates were low (< 30), 12/281 for the Metformin group and 13/273 for the Glibenclamide group".

Intervention and comparison and outcome	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks. Comments without quotation marks from overview review authors
Brown 2017a Glibenclamide versus acarbose **Defined as < 2.2 mmol/L (< 40 mg/dL)**	53 per 1000	**333 per 1000** (46 to 1000)	**RR 6.33** (0.87 to 46.32)	43 (1 RCT)	Low	"There is evidence of selective reporting. Evidence based on one small study with wide confidence intervals. Low event rates and sample size with 8/24 in Glibenclamide group and 1/19 in acarbose group".
Brown 2016a Myo-inositol versus placebo[2] **Not defined**	263 per 1000	**13 per 1000** (0 to 224)	**RR 0.05** (0.00 to 0.85)	73 (1 RCT)	Low	"Evidence is based on one small study with low event rates - 0/35 events in myo-inositol group and 10/38 events in the placebo group".
Han 2017 Energy restricted diet versus no energy restricted diet **Not defined**	190 per 1000	**201 per 1000** (91 to 441)	**RR 1.06** (0.48 to 2.32)	408 (2 RCTs)	Very low	"Evidence is based on two small studies at unclear risk of selection bias; one study at high risk of performance bias and unclear risk of detection bias. Wide confidence intervals crossing the line of no effect and substantial heterogeneity: I^2 = 75% present".
Han 2017 Low-carbohydrate diet versus high-carbohydrate diet **Not defined**	133 per 1000	**121 per 1000** (52 to 283)	**RR 0.91** (0.39 to 2.12)	149 (1 RCT)	Very low	Imprecision - evidence is based on one study and wide confidence interval crossing the line of no effect. Risk of performance bias as participants and researchers were not blinded.
Han 2017 Soy protein-enriched diet versus no soy protein diet **Defined as BGL < 1.7 mmol/L (< 30.6 mg/dL)**	29 per 1000	**88 per 1000** (10 to 806)	**RR 3.00** (0.33 to 27.42)	68 (1 RCT)	Very low	Imprecision - evidence is based on one study and wide confidence interval crossing the line of no effect. Risk of performance bias as participants and personnel were not blinded.
Han 2017 Ethnic specific diet versus standard healthy diet **Not defined**	0 per 1000	**0 per 1000** (0 to 0)	RR not estimable	20 (1 RCT)	Very low	Imprecision - evidence is based on one study. Risk of performance bias as participants and personnel were not blinded and selective reporting (reporting bias). There were no neonatal hypoglycaemic events in either group.
Brown 2017b Lifestyle intervention versus usual care or diet alone **Not defined**	75 per 1000	**74 per 1000** (49 to 114)	**RR 0.99** (0.65 to 1.52)	3000 (6 RCTs)	Moderate	"Allocation concealment was unclear in two trials and blinding was not undertaken in two other trials".
Brown 2017c Exercise versus control **Not defined**	59 per 1000	**118 per 1000** (12 to 1000)	**RR 2.00** (0.20 to 20.04)	34 (1 RCT)	Low	"Imprecision - wide confidence intervals and low event rates. There is a lack of clarity for most items associated with risk of bias".

Intervention and comparison and outcome	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks. Comments without quotation marks from overview review authors
Han 2012 Intensive management versus routine care **Defined as:** **2 studies: < 1.7 mmol/L (< 30.6 mg/dL) in any two consecutive measurements** **1 study: < 1.94 mmol/L (< 35 mg/dL)**	66 per 1000	**26 per 1000** (4 to 167)	**RR 0.39** (0.06 to 2.54)	426 (2 RCTs)	Very low	Evidence is based on two studies with few events and serious/very serious design limitations. Wide confidence intervals crossing the line of no effect and substantial heterogeneity: I^2 = 62%
43.0. Adiposity - neonate						
Brown 2017b Lifestyle intervention versus usual care or diet alone **Defined as: neonatal fat mass (estimated from skinfold thickness)**	Mean Mass: 427 g	**Mean Mass: 37.80 g fewer** (63.97 g fewer to 10.63 g fewer)	**MD -37.30 g** (63.97 to -10.63)	958 (1 RCT)	Low	"Imprecision. Evidence is based on a single trial and there was no blinding of participants/researchers".
51.0 Adiposity - child						
Brown 2017b Lifestyle intervention versus usual care or diet alone **Defined as: Childhood BMI[1] > 85[th] percentile kg/m[2]**	350 per 1000	**318 per 1000** (262 to 388)	**RR 0.91** (0.75 to 1.11)	767 (3 RCTs)	Moderate	"Allocation concealment and randomisation were unclear in 1/3 trials and 1/3 trials did not blind participants/researchers"
Brown 2017b Lifestyle intervention versus usual care or diet alone **Defined as: Childhood BMI[1] z score**	The mean childhood BMI z score was 0.49 lower	The childhood BMI z score in the intervention group was **0.08 lower** (0.28 lower to 10.63 lower)	**MD 0.08** (-0.28 to 0.44)	199 (1 RCT)	Very low	Imprecision - evidence is based on one study and wide confidence interval crossing the line of no effect. Only reports on 199 children of the original trial of 1000 participants.
55.0 Diabetes						
-	-	-	-	-	-	Either no data were reported for this outcome in any of the included Cochrane systematic reviews or none of the included studies in the review pre-specified this outcome.

Intervention and comparison and outcome	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from included reviews in quotation marks. Comments without quotation marks from overview review authors
7.0 Neurosensory disability						
-	-	-	-	-	-	Either no data were reported for this outcome in any of the included Cochrane systematic reviews or none of the included studies in the review pre-specified this outcome.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RCT:** randomised controlled trial; **RR**: risk ratio; **MD:** mean difference

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1]BMI is an acronym for **B**ody **M**ass **I**ndex
[2]4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice

Table 2.10: GRADE Summary of findings table - Health service use

Intervention and comparison and outcome	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
56.0 Number of antenatal visits or admissions						
Han 2017 Soy protein-enriched diet versus no soy protein diet **Defined as maternal hospitalisation**	118 per 1000	**88 per 1000** (21 to 365)	**RR 0.75** (18 to 3.10)	68 (1 RCT)	Very low	Imprecision - evidence based on one trial. Evidence of risk of bias as participants and researchers were not blinded. Wide confidence interval crossing the line of no effect.
Brown 2017b Lifestyle intervention versus usual care or diet alone. **Not defined**	273 per 1000	**289 per 1000** (237 to 352)	**RR 1.06** (0.87 to 1.29)	1000 (1 RCT)	Moderate	Imprecision, evidence is based on a single trial.
61.0 Length of postnatal stay (mother)						
-	-	-	-	-	-	Either no data were reported for this outcome in any of the included Cochrane systematic reviews or none of the included studies in the review pre-specified this outcome.
59.0. Length of postnatal stay (baby) including NICU[1] or SCBU[2]						
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only. **Defined as >4 days**	260 per 1000	**346 per 1000** (190 to 634)	**RR 1.33** (0.73 to 2.44)	99 (1 RCT)	Very low	Imprecision - evidence based on one small trial. Evidence of risk of bias as participants and researchers were not blinded. Wide confidence interval crossing the line of no effect.
61.0 Costs to families associated with the treatment						
-	-	-	-	-	-	Either no data were reported for this outcome in any of the included Cochrane systematic reviews or none of the included studies in the review pre-specified this outcome.
60.0 Costs associated with the treatment						
Brown 2017b Lifestyle intervention versus usual care or diet alone	see comment	see comment	see comment	1000 (1 RCT)	Moderate	One trial in this review included costs associated with the treatment for mild GDM versus usual care and showed costs were higher in the lifestyle intervention group compared to the control group which is mainly due to increased surveillance and increased contact with health professionals. However, the data was not in a suitable format for inclusion in a meta-analysis and therefore summarised in Table 2.20.

Intervention and comparison and outcome	Assumed risk with comparator	Corresponding risk with intervention*	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
61.0 Cost of maternal care						
-	-	-	-	-	-	Either no data were reported for this outcome in any of the included Cochrane systematic reviews or none of the included studies in the review pre-specified this outcome.
61.0 Cost of child (as neonate, child, adult) care						
-	-	-	-	-	-	Either no data were reported for this outcome in any of the included Cochrane systematic reviews or none of the included studies in the review pre-specified this outcome.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: confidence interval; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1]NICU - Neonatal Intensive Care Unit [2]SCBU - Special Care Baby Unit

Table 2.11: Quality assessment table – Maternal – secondary outcomes

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
8.0 Use of additional pharmacotherapy				
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo) **Defined as Insulin**	**RR 0.68** (0.42 to 1.11)	434 (2 RCTs)	Low	Risk of reporting bias for selective reporting. One trial has been registered twice and the population was 93% Hispanic, results may not be generalisable. One trial is only a conference abstract.
Brown 2017a Metformin versus glibenclamide **Defined as Insulin**	**RR 0.66** (0.28 to 1.57)	660 (5 RCTs)	Very low	Risk of performance bias for not blinding participants and personnel in four trials. Risk of reporting bias for selective reporting in three trials. Substantial heterogeneity: $I^2 = 72\%$
Brown 2017a Glibenclamide versus acarbose **Defined as Insulin**	**RR 0.49** (0.19 to 1.27)	43 (1 RCT)	Low	Imprecision - one trial. Evidence of risk of performance bias for not blinding participants and researchers.
Brown 2016a Myo-inositol versus placebo[5] **Defined as Insulin**	**average RR 0.37** (0.08 to 1.73)	157 (2 RCTs)	Low	Wide confidence intervals and risk of reporting bias for selective reporting in one trial and unclear risk of bias for most other areas in the same trial.
Han 2017 Low-moderate GI diet versus moderate-high GI diet **Not defined**	**RR 0.82** (0.39 to 1.74)	221 (4 RCTs)	Low	Evidence of risk of performance bias for not blinding participants and researchers in all trials. One trial had a risk of selection bias for no allocation concealment and one trial had risk of attrition bias for incomplete outcome data.
Han 2017 Energy restricted diet versus no energy restricted diet **Defined as Insulin**	**RR 1.05** (0.47 to 2.34)	117 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval. Risk of reporting bias for selective reporting. The control group had a higher proportion of women with a history of preterm labour.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents **Not defined**	**RR 0.28** (0.14 to 0.53)	86 (2 RCTs)	Moderate	Imprecision- small sample size

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 Low carbohydrate diet versus high-carbohydrate diet **Not defined**	**RR 1.02** (0.77 to 1.37)	180 (2 RCTs)	Low	Risk of performance bias for not blinding participants and personnel in both trials and risk of reporting bias for selective reporting in one trial.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **Not defined**	RR not estimable	111 (2 RCTs)	Low	Risk of performance bias for not blinding participants and personnel. Unbalanced groups at baseline for BMI. There was no use of additional pharmacotherapy in either group.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **Not defined**	**RR 0.83** (0.58 to 1.17)	92 (1 RCT)	Low	Imprecision - one trial. Risk of detection bias for not blinding of outcome assessment, risk of attrition bias for incomplete outcome data and unbalanced groups at baseline for blood glucose concentration.
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only **Not defined**	**RR 0.61** (0.15 to 2.42)	99 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval. Evidence of risk of performance bias for not blinding participants and personnel.
Han 2017 Soy protein-enriched diet versus no soy protein diet **Not defined**	**RR 1.00** (0.15 to 6.70)	68 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval. Risk of performance bias for not blinding participants and personnel.
Han 2017 High-fibre diet versus standard-fibre diet **Not defined**	not estimable	22 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel. There were no events in both groups.
Han 2017 Ethnic specific diet versus standard healthy diet **Not defined**	**RR 2.00** (0.21 to 18.69)	20 (1 RCT)	Very low	Imprecision - one trial. Risk of performance bias for not blinding of participants and personnel and risk of reporting bias for selective reporting.
Brown 2017b Lifestyle intervention versus usual care or diet alone **Defined as oral antidiabetic agents**	**average** **RR 0.79** (0.52 to 1.19)	197 (1 RCT)	Moderate	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Brown 2017b Lifestyle intervention versus usual care or diet alone **Defined as Insulin**	**average** **RR 2.54** (1.19 to 5.42)	3254 (9 RCTs)	Very low	Imprecision - wide confidence intervals. Risk of performance bias for not blinding participants and personnel in four trials. Reporting bias for selective reporting in five trials and substantial heterogeneity: I^2 = 80%.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2017c Exercise versus control **Not defined (insulin in one trial**)	**RR 0.76** (0.54 to 1.08)	413 (7 RCTs)	Moderate	Risk of performance bias for not blinding participants and personnel for three trials and mostly unclear risk of bias assessment for the rest of the trials.
Han 2012 Intensive management versus routine care **Defined as Insulin or oral hypoglycaemic agents**	**RR 1.00** (0.30 to 3.32)	12 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval. Risk of performance bias for not blinding participants and personnel.
Martis 2016a Strict intensity[2] of glycaemic control versus less strict glycaemic control **Defined as Insulin**	**RR 1.85** (1.14 to 3.03)	171 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval. Risk of performance bias for not blinding participants and personnel, risk of reporting bias for selective reporting. Other bias includes no sample size calculation reported, ITT unclear and no protocol has been identified for this trial.
9.0 Maternal hypoglycaemia (as defined in the reviews)				
Brown 2017a Metformin versus glibenclamide **Not defined in two trials** **Third trial defined as < 3.3 mmol/L (60 mg/dL)**	**RR 0.89** (0.36 to 2.19)	354 (3 RCTs)	Low	Imprecision - wide confidence interval. Risk of performance bias for not blinding participants and personnel in two trials.
Brown 2017a Glibenclamide versus acarbose **Not defined**	RR not estimable	43 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel. There were no events for maternal hypoglycaemia in either group.
Han 2017 High-fibre diet versus standard-fibre diet **Not defined**	**MD -1.00** (-2.08 to 0.08)	22 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel. (Recorded as mean numbers of events).
Brown 2017b Lifestyle intervention versus usual care or diet alone **Not defined**	RR not estimable	19 (1 RCT)	Very low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting. Unbalanced groups at baseline for 1-hour plasma glucose in diagnostic test. There were no events for maternal hypoglycaemia in either group.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2017c Exercise versus control **Not defined**	RR not estimable	34 (1 RCT)	Low	Imprecision - one trial with small number. There were no events for maternal hypoglycaemia in either group.
10.1 Glycaemic control: timing not defined				
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **Timing or test not defined**	**MD -0.10** mmol/L (-0.38 to 0.18)	74 (1 RCT)	Very low	Imprecision - one trial. Risk of detection bias for not blinding of outcome assessment, risk of attrition bias for incomplete outcome data and unbalanced groups at baseline for blood glucose concentration.
10.2 Glycaemic control *during* the treatment: pre-prandial/fasting				
Han 2017 Energy restricted diet versus no energy restricted diet **During not defined**	**MD 0.21** mmol/L (-0.58 to -0.99)	311 (2 RCTs)	Low	Imprecision - wide confidence interval. Risk of performance bias for not blinding participants and personnel in one trial and unclear risk of bias for five out of seven risk of bias assessments in one trial.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **During defined as at 38 weeks gestation**	**MD 0.50** mmol/L (0.30 to 0.70)	24 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel. Unbalanced groups at baseline for BMI.
10.3 Glycaemic control *during* the treatment: post-prandial				
Han 2017 Energy restricted diet versus no energy restricted diet **During not defined but at one hour post-prandial**	**MD -0.25** mmol/L (-0.68 to -0.18)	299 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **During defined as at 38 weeks gestation and post-prandial time not defined**	**MD 0.90** mmol/L (0.58 to 1.22)	25 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel. Unbalanced at baseline for BMI.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
10.4 Glycaemic control *during* treatment: HbA1c (haemoglobin A1c or glycated haemoglobin)				
Brown 2017a Metformin versus glibenclamide **During defined as third trimester**	**SMD -0.12** (-0.39 to 0.16)	200 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **At 38 weeks gestation**	**MD 0.40 %** (0.32 to 0.48)	25 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel. Unbalanced groups at baseline for BMI.
10.5 Glycaemic control *during* the treatment: 24 hour mean plasma glucose				
Han 2017 Energy restricted diet versus no energy restricted diet **During not defined**	**MD 0.10** mmol/L (-0.82 to 1.02)	12 (1 RCT)	Low	Imprecision - one trial. Unclear risk of bias for five out of seven risk of bias assessments.
10.6 Glycaemic control at the *end* of treatment: Fasting				
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo) **Blood glucose concentration taken at the last three antenatal visits**	**MD -3.0** mg/dL (-5.13 to -0.87)	375 (1 RCT)	Low	Imprecision - one trial with wide confidence interval. Risk of reporting bias for selective reporting.
Brown 2017a Metformin versus glibenclamide **Defined as blood glucose concentration**	**SMD 0.19** mmol/L (0.02 to 0.37)	508 (3 RCTs)	Low	Imprecision - wide confidence intervals. Risk of performance bias for not blinding participants and personnel.
Brown 2016a Myo-inositol versus placebo[5] **Tested with OGGT[4]**	**MD -0.47** mmol/L (-0.59 to -0.35)	142 (2 RCTs)	Moderate	Risk of reporting bias for selective reporting in one trial and unclear risk of bias in four assessments in the same trial.
Han 2017 Low-moderate GI diet versus moderate-high GI diet **Defined as blood glucose concentration**	**MD -0.15** mmol/L (-0.55 to 0.25)	83 (1 RCT)	Very low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel and risk of selection bias for no allocation concealment.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 Energy restricted diet versus no energy restricted diet **Defined as blood glucose concentration**	**MD -0.23** mmol/L (-0.44 to -0.03)	311 (2 RCTs)	Low	Imprecision - wide confidence intervals. Risk of performance bias for not blinding participants and personnel in one trial and unclear risk of bias for five out of seven risk of bias assessments in one trial.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents **Defined as blood glucose concentration**	**MD -0.42** mmol/L (-0.53 to -0.32)	66 (2 RCTs)	Moderate	Imprecision due to small sample size
Han 2017 Low carbohydrate diet versus high-carbohydrate diet **Defined as blood glucose concentration**	**MD 5.00** mg/dL (-0.01 to 10.01)	30 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **Defined as blood glucose concentration**	**MD 0.18** mmol/L (-0.17 to 0.53)	84 (1 RCT)	Low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Diet recommendation + diet-related behavioural advice versus diet **Defined as blood glucose concentration**	**MD 0.0** mg/dL (-4.25 to 4.25)	99 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Soy protein-enriched diet versus no soy protein diet **Defined as blood glucose concentration**	**MD -10.60** mg/dL (-15.37 to -5.83)	68 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval. Risk of performance bias for not blinding participants and personnel.
Brown 2017c Exercise versus control	**SMD -0.59** (-1.07 to -0.11)	363 (4 RCTs)	Low	Heterogeneity: I^2 = 73% and the risk of bias assessment for most trials are mainly unclear.
10.7 Glycaemic control at the *end* of treatment: One hour post-prandial				
Brown 2016a Myo-inositol versus placebo[5] **Tested with OGGT[4]**	**MD -0.90** mmol/L (-1.73 to -0.07)	73 (1 RCT)	Moderate	Imprecision - one trial with small numbers.
Han 2017 Energy restricted diet versus no energy restricted diet **Blood glucose concentration**	**MD -0.51** mmol/L (-0.89 to -0.13)	299 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2017b Lifestyle intervention versus usual care or diet alone **Blood glucose concentration:** **One hour post-prandial in two trials;** **Two hours post-prandial in two trials;** **One trial timing not defined**	**average** **MD -27.11** mg/dL (-44.62 to -9.61)	588 (4 RCTs)	Very low	Imprecision - wide confidence intervals. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
10.8 Glycaemic control at the *end* of treatment: Two hours post-prandial				
Brown 2017a Metformin versus glibenclamide **Blood glucose concentration: after dinner where specified**	**SMD 0.16** mmol/L and mg/dL (-0.01 to 0.34)	508 (3 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Brown 2016a Myo-inositol versus placebo[5] **Tested with OGTT[4]**	**MD -0.70** mmol/L (-1.46 to 0.06)	73 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect.
Han 2017 Low-moderate GI diet versus moderate-high GI diet **Blood glucose concentration**	**MD -0.71** mmol/L (-1.21 to -0.21)	83 (1 RCT)	Very low	Imprecision - one trial with small numbers. Risk of performance bias for not blinding participants and personnel and risk of selection bias for no allocation concealment.
Han 2017 Low carbohydrate diet versus high-carbohydrate diet **Blood glucose concentration after breakfast**	**MD 6.00** mg/dL (-1.47 to 13.47)	30 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Low carbohydrate diet versus high-carbohydrate diet **Blood glucose concentration after lunch**	**MD 3.00** mg/dL (-2.77 to 8.77)	30 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Low carbohydrate diet versus high-carbohydrate diet **Blood glucose concentration after dinner**	**MD 6.00** mg/dL (-1.47 to 13.47)	30 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **Blood glucose concentration**	**MD -0.02** mmol/L (-0.29 to 0.25)	84 (1 RCT)	Low	Imprecision - one trial with small numbers. Risk of performance bias for not blinding participants and personnel.
10.9 Glycaemic control at the *end* of treatment: Post-prandial timing not defined				
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only **Blood glucose concentration**	**MD -9.30** mg/dL (-15.58 to -3.02)	99 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel.
Brown 2017c Exercise versus control **Blood glucose concentration**	**SMD -0.85** (-1.15, -0.55)	344 (3 RCTs)	Moderate	Most of the risk of bias assessments in the trials unclear and one trial had risk of performance bias for not blinding participants and personnel.
Brown 2017c Exercise versus control **OGTT**[4]	**MD -81.60** mg/dL (-96.03 to -67.17)	19 (1 RCT)	Low	Imprecision - one trial with small numbers. Six out of seven risk of bias assessments in the trial are unclear.
10.10 Glycaemic control at the *end* of treatment: mean plasma glucose				
Han 2017 Energy restricted diet versus no energy restricted diet **in 24 hours**	**MD -1.30** mmol/L (-2.25 to -0.35)	12 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval. Risk of bias unclear for five risk of bias assessments.
Brown 2017c Exercise versus control	**MD 0.28** mmol/L (0.04 to 0.52)	34 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval and small numbers. Risk of attrition bias for incomplete outcome data and unclear for the other risk of bias assessments.
10.11 Glycaemic control at the *end* of treatment: HbA1c (haemoglobin A1c or glycated haemoglobin)				
Han 2017 Low-moderate GI diet versus moderate-high GI diet	**MD 0.01** % (-0.18 to 0.20)	83 (1 RCT)	Very low	Imprecision - one trial with small numbers. Risk of selection bias for no allocation concealment and risk of performance bias for not blinding participants and personnel.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents	**MD -0.25** % (-0.76 to 0.26)	34 (1 RCT)	Moderate	Imprecision - one trial with small numbers.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only	**MD -0.10** % (-0.28 to 0.08)	99 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Brown 2017b Lifestyle intervention versus usual care or diet alone	average **MD -0.33** mmol/mol (-0.47 to -0.19)	532 (6 RCTs)	Very low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel in 3 trials and risk of reporting bias for selective reporting in 4 trials. Substantial heterogeneity: I^2 = 92%
Brown 2017c Exercise versus control	**MD -0.43** mmol/mol (-0.51 to -0.35)	320 (2 RCTs)	High	All risk of bias assessments unclear in one trial.
10.12 Glycaemic control *during/at the end* of treatment: Fasting				
Han 2017 Energy restricted diet versus no energy restricted diet	**MD 0.10** mmol/L (-0.18 to -0.38)	117 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**average** **MD -3.10** mg/dL (-7.01 to 0.81)	853 (6 RCTs)	Very low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel risk of reporting bias for selective reporting for most trails. Substantial heterogeneity: I^2 = 92%
10.13 Glycaemic control *during/at the end* of treatment: Mean plasma glucose				
Han 2017 Energy restricted diet versus no energy restricted diet	**MD 0.10** mmol/L (-0.34 to -0.54)	117 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting.
Han 2017 High-fibre diet versus standard-fibre diet	**MD 0.0** mmol/L (-8.26 to 8.26)	22 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
10.14 Glycaemic control *during/at the end* of treatment: Mean HbA1c				
Han 2017 Energy restricted diet versus no energy restricted diet	**MD -0.20** % (-0.64 to -0.24)	117 (1 RCT)	Low	Imprecision - one trial. Risk of reporting bias for selective reporting.
11.0 Weight gain in pregnancy				
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo)	**MD 0.0** kg (-0.96 to 0.96)	375 (1 RCT)	Low	Imprecision - one trial. Risk of reporting bias for selective reporting.
Brown 2017a Metformin versus glibenclamide	**MD -2.06** kg (-3.98 to -0.14)	200 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval. Risk of reporting bias for selective reporting.
Brown 2017a Glibenclamide versus acarbose	**MD -0.60** kg (-3.13 to -1.93)	43 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel.
Brown 2016a Myo-inositol versus placebo[5]	**MD -0.50** kg (-3.35 to 2.25)	69 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting and unclear risk of bias for four other risk assessments.
Han 2017 Low-moderate GI diet versus moderate-high GI diet	**MD -0.47** kg (-2.18 to 1.24)	83 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of selection bias for no allocation concealment and risk of performance bias for not blinding participants and personnel.
Han 2017 Energy restricted diet versus no energy restricted diet	**MD 1.88** kg (-1.96 to 5.72)	117 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents	**MD -2.88** kg (-8.48 to 2.71)	66 (2 RCTs)	Moderate	Imprecision - wide confidence interval crossing the line of no effect.
Han 2017 Low-carbohydrate diet versus high-carbohydrate diet	**MD -0.90** kg (-1.60 to -0.20)	145 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories	**MD -1.98** kg (-4.32 to 0.36)	84 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet	**MD -1.20** kg (-3.43 to 1.03)	87 (1 RCT)	Very low	Imprecision - one trial. Risk of detection bias for not blinding of outcome assessment, risk of attrition bias for incomplete outcome data and unbalanced groups at baseline for blood glucose concentration.
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only	**MD -0.10** kg (-4.91 to 4.71)	99 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Soy protein-enriched diet versus no soy protein diet	**MD 3.50** kg (-1.47 to 8.47)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 High-fibre diet versus standard-fibre diet	**MD 2.40** kg (-2.20 to 7.00)	22 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Ethnic specific diet versus standard healthy diet	**MD -2.20** kg (-7.24 to 2.84)	20 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete outcome data.
Brown 2017b Lifestyle intervention versus usual care or diet alone	average **MD -1.30** kg (-2.26 to -0.35)	2930 (4 RCTs)	Moderate	Substantial heterogeneity: $I^2 = 80\%$
Brown 2017c Exercise versus control	**MD -0.34** (-1.25 to 0.58)	104 (2 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel in one trial and unclear risk of bias assessments in five out of seven for second trial.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2012 Intensive management versus routine care	**MD -0.63** kg (-3.07 to 1.81)	426 (2 RCTs)	Very low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete outcome data.
12.0 Other measures of weight gain in pregnancy (not prespecified for this overview)				
Brown 2016a Myo-inositol versus placebo[5] **BMI during pregnancy**	**MD -1.50** kg/m^2 (-2.35 to -0.65)	73 (1 RCT)	Moderate	Imprecision - one trial.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents **BMI at the end of the pregnancy**	**MD -0.83** kg/m^2 (-3.76 to 2.11)	66 (2 RCTs)	Moderate	Imprecision - wide confidence interval crossing the line of no effect.
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only **BMI at the end of the pregnancy**	**MD -0.0** kg/m^2 (-1.75 to 1.75)	99 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Soy protein-enriched diet versus no soy protein diet **BMI at the end of the pregnancy**	**MD 0.60** kg/m^2 (-1.43 to 2.63)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Brown 2017c Exercise versus control **Excessive weight gain in pregnancy**	**RR 0.90** (0.47, 1.72)	79 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. All risk of bias assessments are unclear.
13.0 Adherence to the intervention				
Han 2017 Low-carbohydrate diet versus high-carbohydrate diet **Adherence not defined**	**RR 1.09** (0.73 to 1.62)	30 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **Assessed by a 24-hour recall when women were attending their dietitian appointment**	**RR 0.84** (0.64 to 1.11)	92 (1 RCT)	Very low	Imprecision - one trial. Risk of detection bias no blinding of outcome assessment and risk of attrition bias for incomplete outcome data. Unbalanced groups at baseline for blood glucose concentration at diagnosis of GDM.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 Ethnic specific diet versus standard healthy diet **Assessed using a 24-hour food intake recall method;** women with an intake of more than 20% higher than prescribed received a score of 0; those with an intake of 10% to 20% higher received a score of 1; and women with intake consistent with the plan or up to 10% lower received a score of 2. 'Good adherence' was defined as women being scored a 1 or 2	**RR 3.50** (0.95 to 12.90)	20 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Brown 2017c Exercise versus control	**RR 1.00** (0.83 to 1.21)	19 (1 RCT)	Low	Imprecision - one trial with small numbers. Six out of seven risk of bias assessments are unclear.
15.0 Placental abruption				
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents	**RR 3.00** (0.13 to 70.73)	58 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval. Unclear risk of selection bias, performance bias, detection bias and reporting bias.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories	RR not estimable	27 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel. There were no events in either group. Unbalanced groups at baseline for BMI.
16.0 Postpartum haemorrhage (PPH) (as defined in the reviews)				
Han 2017 Low-moderate GI diet versus moderate-high GI diet **PPH not defined**	**RR 1.02** (0.15 to 6.93)	83 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel and risk of selection bias for no allocation concealment.
Brown 2017b Lifestyle intervention versus usual care or diet alone **PPH not defined**	**average RR 0.61** (0.20 to 1.89)	1165 (2 RCTs)	Low	Risk of performance bias for not blinding participants and personnel. Heterogeneity: $I^2 = 64\%$

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
17.0 Postpartum infection				
Han 2017 Low-moderate GI diet versus moderate-high GI diet	**RR 0.34** (0.01 to 8.14)	83 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel and risk of selection bias for no allocation concealment.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 0.61** (0.34 to 1.10)	1000 (1 RCT)	Moderate	Imprecision - one trial.
19.1 Breastfeeding at discharge				
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 1.04** (0.99 to 1.10)	1000 (1 RCT)	Moderate	Imprecision - one trial.
19.1.2 Breastfeeding at six weeks postpartum				
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 0.97** (0.87 to 1.07)	188 (1 RCT)	Very low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
19.1.3 Breastfeeding at six months postpartum or longer				
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 1.31** (0.99 to 1.74)	161 (1 RCT)	Very low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
20.0 Maternal mortality				
Brown 2017c Exercise versus control	RR not estimable	48 (2 RCTs)	Very low	Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data outcome in one trial and unclear risk of bias for most of the assessments in both trials. There were no events in either group.
21.1 Sense of well-being and quality of life *during* treatment: Overall physical component				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Short Form Health Survey (SF-36)**	**MD 1.5** (0.12 to 2.88)	682 (1 RCT)	Low	Imprecision - one trial with wide confidence interval.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
21.2 Sense of well-being and quality of life *during* treatment: Overall mental component				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Short Form Health Survey (SF-36)**	**MD 1.30** (-0.17 to 2.77)	682 (1 RCT)	Low	Imprecision - one trial with wide confidence interval crossing the line of no effect.
21.3 Sense of well-being and quality of life *during* treatment: Anxiety				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Short Form Health Survey (SF-36)**	**MD -0.30** (-0.88 to 0.28)	682 (1 RCT)	Moderate	Imprecision - one trial.
21.4 Sense of well-being and quality of life at *three months* post-partum: Overall physical component				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Short Form Health Survey (SF-36)**	**MD 1.20** (-0.19 to 2.59)	573 (1 RCT)	Low	Imprecision - one trial with wide confidence interval crossing the line of no effect.
21.5 Sense of well-being and quality of life at *three months* post-partum: Overall mental component				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Short Form Health Survey (SF-36)**	**MD 0.20** (-1.51 to 1.91)	573 (1 RCT)	Low	Imprecision - one trial with wide confidence interval crossing the line of no effect.
21.6 Sense of well-being and quality of life at *three months* post-partum: Anxiety				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Short Form Health Survey (SF-36)**	**MD -0.20** (-0.83 to 0.43)	573 (1 RCT)	Low	Imprecision - one trial with wide confidence interval crossing the line of no effect.
22.0 Women's view of the intervention				
Brown 2017c Exercise versus control	Women reported favourable views but MD SD not estimable	40 (1 RCT)	Low	Imprecision - one trial with small numbers. Five out of seven risk of bias assessments are unclear.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
23.1 Homeostasis Model Assessment Insulin Resistance (HOMA-IR) and (HOMA2-IR up-dated version)				
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents **Measured with HOMA-IR at the end of the intervention**	**MD -1.00** % (-1.34 to -0.66)	32 (1 RCT)	Moderate	Imprecision - one trial.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **Measured with HOMA2-IR at the end of the intervention**	**MD -0.10** % (-0.38 to 0.18)	77 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence intervals crossing the line of no effect. Risk of detection bias for no blinding of outcome assessment and risk of attrition bias for incomplete outcome data.
Hans 2017 Low-GI diet versus high-fibre moderate-GI diet **Measured with HOMA-IR at three months postpartum**	**MD -0.30** % (-0.66 to 0.06)	53 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence intervals crossing the line of no effect. Risk of detection bias for no blinding of outcome assessment and risk of attrition bias for incomplete outcome data.
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only **Measured with HOMA-IR at the end of the intervention**	**MD -0.30** % (-0.77 to 0.17)	99 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Soy protein-enriched diet versus no soy protein diet **Measured with HOMA-IR at the end of the intervention**	**MD -1.60** % (-2.20 to 0.20)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
23.2 Quantitative Insulin Sensitivity Check Index (QUICKI)				
Han 2017 Soy protein-enriched diet versus no soy protein diet **Measured at the end of the intervention**	**MD 0.0** (-0.01 to 0.01)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
23.3 Fasting plasma insulin *during* the intervention				
Han 2017 Energy restricted diet versus no energy restricted diet **During (gestation) not defined**	**MD 100.00** pM[3] (-26.02 to 226.02)	12 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence intervals crossing the line of no effect. Risk of bias unclear for five risk of bias assessments.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **Measured at 38 weeks gestation**	**MD 4.40** mU/L (2.59 to 6.21)	24 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence intervals. Risk of performance bias for not blinding participants and personnel. Unbalanced groups at baseline for BMI.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **Measured in 10^{-5} min^{-1} per mU/L min at 38 weeks gestation**	**MD -0.08** mU/L min (-0.21 to 0.05)	24 (1 RCT)	Very low	Imprecision - one trial with small numbers. Risk of performance bias for not blinding participants and personnel. Unbalanced groups at baseline for BMI.
23.4 Fasting plasma insulin *end* of intervention				
Han 2017 Energy restricted diet versus no energy restricted diet	**MD -20.00** pM^3 (-127.70 to 87.70)	12 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence intervals. Risk of bias unclear for five risk of bias assessments.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents	**MD -3.26** µIU/mL (-4.42 to -2.10)	32 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet	**MD 10.80** pmol/L (-22.36 to 43.96)	70 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence intervals. Risk of detection bias for not blinding outcome assessment and risk of attrition bias for selective reporting.
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only	**MD -0.50** µIU/mL (-2.69 to 1.69)	99 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Soy protein-enriched diet versus no soy protein diet	**MD -2.60** µIU/mL (-8.03 to 2.83)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.

CI: confidence interval; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

*__GRADE ratings of evidence__
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] DASH is an acronym for Dietary Approaches to Stop Hypertension
[2]Strict intensity of glycaemic control (stricter) defined in review as: pre-prandial 5.0 mmol/L (90 mg/dL) and one hour post-prandial 6.7 mmol/L (120 mg/dL) and less strict glycaemic control (liberal) defined in review as: pre-prandial 5.8 mmol/L (104 mg/dL) and one hour post-prandial 7.8 mmol/L (140 mg/dL)
[3]pM is the same as pmol/L
[4]OGTT is an acronym for Oral Glucose Tolerance Test
[5]4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice

Table 2.12: Quality assessment table - Maternal *long term* - secondary outcomes

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
26.0 Body Mass Index (BMI)				
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **BMI at three months**	**MD -0.50** kg/m^2 (-2.79 to 1.79)	52 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of detection bias for not blinding of outcome assessment and risk of attrition bias for incomplete outcome data. Unbalanced groups at baseline for blood glucose concentration at diagnosis of GDM.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **BMI at five to nine months**	**MD 4.10** kg/m^2 (2.34 to 5.86)	27 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel. Unbalanced groups at baseline for BMI.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
28.0 Impaired glucose tolerance				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Test and timing not defined**	**RR 0.67** (0.12 to 3.69)	56 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of reporting bias for selective reporting.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **Borderline OGTT[1] one to two weeks postpartum**	**RR 1.50** (0.30 to 7.43)	24 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel. Unbalanced groups at baseline for BMI.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **At three months post-partum, test not defined**	**RR 1.33** (0.44 to 4.04)	58 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of detection bias not blinding of outcome assessment and risk of attrition bias for incomplete outcome data.
Brown 2017b Lifestyle intervention versus usual care or diet alone **Fasting plasma glucose at three months post-partum**	**MD -0.08** mmol/L (-0.16 to 0.00)	165 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel.
Brown 2017b Lifestyle intervention versus usual care or diet alone **Fasting plasma glucose at six months post-partum**	**MD -0.14** mmol/L (-0.22 to -0.06)	165 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias as no blinding of participants and personnel.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **Borderline OGTT[1] four to 13 months post-partum**	**RR 0.27** (0.01 to 4.93)	7 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel. Unbalanced groups at baseline for BMI.
29.0 Cardiovascular health (as defined in the reviews including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Defined as metabolic syndrome at 4.5 to 10 years follow-up**	**RR 0.93** (0.71 to 1.22)	430 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel.

CI: confidence interval; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

*__GRADE ratings of evidence__
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1]OGTT is an acronym for Oral Glucose Tolerance Test

Table 2.13: Quality assessment table - Fetal/neonatal - secondary outcomes

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
31.0 Stillbirth				
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo)	**RR 0.49** (0.05 to 5.38)	375 (1 RCT)	Very low	Imprecision- one trial with wide confidence interval crossing the line of no effect. Low event rates. Risk of reporting bias for selective reporting. The population was 93% Hispanic, results may not be generalisable. No published protocol was found.
Brown 2017a Metformin versus glibenclamide	**RR 0.92** (0.06 to 14.55)	200 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2017 Energy restricted diet versus no energy restricted diet	RR not estimable	423 (2 RCTs)	Low	Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting. There were no events in either group.
Han 2017 Low-carbohydrate diet versus high-carbohydrate diet	**RR 3.00** (0.12 to 72.49)	150 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome		Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2017b Lifestyle intervention versus usual care or diet alone		**RR 0.15** (0.01 to 2.86)	2355 (4 RCTs)	Very low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel in one trial and risk of reporting bias for selective reporting in two trials.
Brown 2017c Exercise versus control		RR not estimable	29 (1 RCT)	Very low	Imprecision - one trial with low numbers. Risk of performance bias as no blinding of participants and risk of attrition bias for incomplete outcome data. There were no events in either group.
32.0 Neonatal death					
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo)		RR not estimable	375 (1 RCT)	Very low	Imprecision - one trial. The population was 93% Hispanic, results may not be generalisable. Risk of reporting bias for selective reporting, no published protocol was found. The trial appears to be registered twice with the same outcomes. There were no events of neonatal deaths reported in either group.
Han 2017 Energy restricted diet versus no energy restricted diet		RR not estimable	423 (2 RCTs)	Low	Risk of performance bias for not blinding participants and personnel. There were no events of stillbirths reported in either group.
Brown 2017b Lifestyle intervention versus usual care or diet alone		**RR 0.73** (0.22 to 2.42)	3055 (5 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel in one trial, risk of reporting bias for selective reporting in four trials and risk of attrition bias for incomplete outcome data in one trial.
33.0 Macrosomia (> 4000 g; or as defined in the reviews)					
Boulvain 2001 Induction of labour versus expectant management	**> 4000 g**	**RR 0.56** (0.32 to 0.98)	200 (1 RCT)	Very low	Imprecision - one trial. Unclear risk of bias for all assessments.
Brown 2017a Glibenclamide versus placebo	**≥ 4000 g**	**RR 0.71** (0.36 to 1.41)	375 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting, no published protocol was found. The population was 93% Hispanic, results may not be generalisable. The trial appears to be registered twice with the same outcomes.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2017a Metformin versus glibenclamide **≥ 4000 g (one trial) ≥ 3700 g (one trial)**	**RR 0.72** (0.23 to 2.21)	308 (2 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Brown 2017a Glibenclamide versus acarbose **> 4000 g**	**RR 7.20** (0.41 to 125.97)	43 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel.
Han 2017 Low-moderate GI diet versus moderate-high GI diet **> 4000 g**	**RR 0.59** (0.16 to 2.26)	172 (3 RCTs)	Very low	Imprecision - one trial with wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of selection bias for no allocation concealment.
Han 2017 Energy restricted diet versus no energy restricted diet **> 4000 g**	**RR 0.99** (0.64 to 1.53)	421 (2 RCTs)	Very low	Wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2017 Energy restricted diet versus no energy restricted diet **> 4500 g**	**RR 1.01** (0.33 to 3.05)	299 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents **≥ 4000 g**	**RR 0.10** (0.01 to 0.73)	52 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Unclear risk of bias for four assessments.
Han 2017 Low-carbohydrate diet versus high-carbohydrate diet **> 4000 g**	**RR 0.20** (0.02 to 1.69)	179 (2 RCTs)	Low	Imprecision - one trial with wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **> 4000 g**	**RR 0.53** (0.18 to 1.56)	111 (2 RCTs)	Low	Imprecision - one trial with wide confidence intervals crossing the line of no effect. Risk of performance bias for no blinding of participants and personnel. Unbalanced groups at baseline for BMI.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **> 4000 g**	**RR 0.32** (0.03 to 2.96)	92 (1 RCT)	Very low	Imprecision - one trial wide confidence intervals. Risk of detection bias for not blinding outcome assessment and risk of attrition bias for incomplete data.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 Soy protein-enriched diet versus no soy protein diet **> 4000 g**	**RR 0.60** (0.16 to 2.31)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Ethnic specific diet versus standard healthy diet **> 4000 g**	**RR 0.20** (0.01 to 3.70)	20 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data.
Brown 2017b Lifestyle intervention versus usual care or diet alone **> 4 kg (five trials)** **≥ 4 kg (two trials)**	**average RR 0.64** (0.48 to 0.87)	3422 (7 RCTs)	Low	Risk of performance bias for not blinding participants and personnel in three trials. Risk of reporting bias for selective reporting in three trials. Risk of attrition bias for incomplete data in one trial. Heterogeneity: I^2= 65%
Brown 2017c Exercise versus control **not defined**	**RR 0.69** (0.35 to 1.35)	296 (5 RCTs)	Moderate	Risk of performance bias for not blinding participants and personnel in two trials and risk of attrition bias for incomplete data in two trials.
Han 2012 Intensive management versus routine care **≥ 4000 g**	**RR 0.38** (0.19 to 0.74)	438 (3 trials)	Moderate	Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data.
Martis 2016a Strict intensity of glycaemic control[2] versus less strict glycaemic control **> 4000 g**	**RR 1.35** (0.31 to 5.85)	171 (1 RCT)	Very low	Imprecision - one trial with wide confidence intervals. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
34.0 Small-for-gestational age (SGA) (as defined in the reviews)				
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo) **not defined**	**RR 1.11** (0.58 to 2.10)	375 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting, no published protocol was found. The population was 93% Hispanic, results may not be generalisable. The trial appears to be registered twice with the same outcomes.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2017a Glibenclamide versus acarbose **not defined**	RR not estimable	43 (1 RCT)	Low	Imprecision - one trial with small numbers. Risk of performance bias for not blinding participants and personnel. There were no events reported in either group.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **not defined**	**RR 5.16** (0.26 to 103.27)	63 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Low-carbohydrate diet versus high-carbohydrate diet **not defined**	**RR 0.68** (0.29 to 1.56)	149 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **not defined**	**RR 1.20** (0.34 to 4.18)	92 (1 RCT)	Very low	Imprecision - one trial with wide confidence intervals crossing the line of no effect. Risk of detection bias for no blinding of outcome assessments and risk of attrition bias for incomplete outcome data.
Han 2017 Ethnic specific diet versus standard healthy diet **not defined**	**RR 0.33** (0.02 to 7.32)	20 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data.
Brown 2017b Lifestyle intervention versus usual care or diet alone **not defined**	**RR 0.98** (0.73 to 1.32)	2324 (4 RCTs)	Moderate	Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2012 Intensive management versus routine care **not defined**	**RR 1.53** (0.81 to 2.88)	509 (3 RCTs)	Very low	Imprecision - one trial with wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data.
Martis 2016a Strict intensity of glycaemic control[2] versus less strict glycaemic control **not defined**	**RR 1.12** (0.48 to 2.63)	171 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
35.1 Birth trauma not defined				
Brown 2017a Metformin versus glibenclamide	RR not estimable	159 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel. There were no events either group.
Brown 2017a Glibenclamide versus acarbose	RR not estimable	43 (1 RCT)	Low	Imprecision - one trial with small numbers. Risk of performance bias for not blinding participants and personnel. There were no events reported in either group.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 0.48** (0.12 to 1.90)	1930 (3 RCTs)	Low	Risk of performance bias for not blinding participants and personnel in one trial. Risk of reporting bias for selective reporting in two trials and risk of attrition bias for incomplete outcome data.
35.2 Birth trauma: Shoulder dystocia				
Boulvain 2001 Induction of labour versus expectant management Induction at 38 completed weeks for all women	**RR 0.14** (0.01 to 2.73)	200 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Rik of bias for all assessments unclear, as not reported in the review. There were three babies with shoulder dystocia in the expectant management group and none in the intervention group.
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo)	**RR 0.33** (0.01 to 8.00)	375 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting, no published protocol was found. The population was 93% Hispanic, results may not be generalisable. The trial appears to be registered twice with the same outcomes.
Brown 2017a Metformin versus glibenclamide	**RR 0.99** (0.14 to 6.89)	195 (2 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel in one trial and risk of reporting bias for selective reporting in one trial.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 Energy restricted diet versus no energy restricted diet	**RR 0.12** (0.01 to 2.26)	418 (2 RCTs)	Very low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2012 Intensive management versus routine care	**RR 0.69** (0.06 to 7.27)	83 (1 RCT)	Very low	Imprecision - one trial with wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel, risk of attrition bias for incomplete data and risk of reporting bias for selective reporting.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 0.38** (0.21 to 0.66)	2894 (5 RCTs)	Low	Risk of attrition bias for incomplete outcome data in one trial, risk of performance bias for not blinding participants and personnel in two trials and risk of reporting bias for selective reporting in two trials
35.3 Birth trauma: Bone fracture				
Boulvain 2001 Induction of labour versus expectant management	RR not estimable	200 (1 RCT)	Very low	Imprecision - one trial. Risk of bias for all assessments unclear, as not reported in the review. There were no events reported in either group.
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo)	**RR 0.74** (0.17 to 3.25)	375 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting, no published protocol was found. The population was 93% Hispanic, results may not be generalisable. The trial appears to be registered twice with the same outcomes.
Han 2017 Energy restricted diet versus no energy restricted diet	RR not estimable	299 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel. There were no events reported in either group.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 0.35** (0.01 to 8.45)	1730 (2 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of attrition bias for incomplete outcome data in one trial and risk of reporting bias for selective reporting in one trial. Event rates were very low with only one bone fracture reported in the control group.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
35.4 Birth trauma: Nerve palsy (brachial plexus)				
Boulvain 2001 Induction of labour versus expectant management	RR not estimable	200 (1 RCT)	Very low	Imprecision - one trial. Risk of bias for all assessments unclear, as not reported in the review. There were no events reported in either group.
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo)	**RR 0.33** (0.01 to 8.00)	375 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting, no published protocol was found. The population was 93% Hispanic, results may not be generalisable. The trial appears to be registered twice with the same outcomes.
Han 2017 Energy restricted diet versus no energy restricted diet	RR not estimable	299 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel. There were no events reported in either group.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 0.15** (0.01 to 2.86)	1030 (1 RCT)	Low	Imprecision - one trial with wide confidence intervals crossing the line of no effect. Three babies reported with nerve palsy in the control group.
36.0 Gestational age at birth				
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo)	**MD 0.0** weeks (-0.32 to 0.32)	375 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting, no published protocol was found. The population was 93% Hispanic, results may not be generalisable. The trial appears to be registered twice with the same outcomes.
Brown 2017a Metformin versus glibenclamide	**MD 0.03** weeks (-0.22 to 0.28)	508 (3 RCTs)	Very low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Brown 2017a Glibenclamide versus acarbose	**MD -0.10** weeks (-0.82 to 0.62)	43 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2016a Myo-inositol[3] versus placebo	**MD 2.1** weeks (1.27 to 2.93)	73 (1 RCT)	Moderate	Imprecision - one trial.
Han 2017 Low-moderate GI diet versus moderate-high GI diet	**MD 0.30** weeks (-0.30 to 0.90)	62 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Energy restricted diet versus no energy restricted diet	**MD -0.16** weeks (-0.67 to 0.36)	423 (2 RCTs)	Moderate	Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents	MD 0.20 weeks (-0.45 to 0.85)	52 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Unclear risk of bias for four other risk of bias assessments.
Han 2017 Low-carbohydrate diet versus high-carbohydrate diet	MD 0.10 weeks (-0.42 to 0.62)	180 (2 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories	**MD 0.25** weeks (-0.51 to 1.01)	111 (2 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel. Unbalanced groups at baseline for BMI.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet	**MD -0.10** (-0.39 to 0.19)	92 (1 RCT)	Low	Imprecision - one trial with small numbers. Risk of detection bias for not blinding outcome assessments and risk of attrition bias for incomplete outcome data.
Han 2017 Soy protein-enriched diet versus no soy protein diet	**MD 0.40** weeks (-0.23 to 1.03)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 High-fibre diet versus standard-fibre diet	**MD 0.0** weeks (-1.30 to 1.30)	22 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 Ethnic specific diet versus standard healthy diet	**MD -0.40** weeks (-1.15 to 0.35)	20 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**MD 0.04** weeks (-0.13 to 0.20)	2057 (5 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel in one trial, risk of attrition bias for incomplete data in one trial and risk of reporting bias for selective reporting in four trials.
Brown 2017c Exercise versus control	**MD -0.01** weeks (-0.40 to 0.38)	167 (4 RCTs)	Low	Risk of performance bias for not blinding participants and personnel in two trials and risk of attrition bias for incomplete data in two trials. Unclear risk of bias assessment in most trials for all other risk of bias assessments.
Han 2012 Intensive management versus routine care	**MD -0.18** weeks (-0.43 to 0.07)	521 (4 RCTs)	Very low	Imprecision - one trial with wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data.
Martis 2016a Strict intensity of glycaemic control[2] versus less strict glycaemic control	**MD -0.30** weeks (-0.73 to 0.13)	171 (1 RCT)	Very low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
37.0 Preterm birth (< 37 weeks' gestation and < 32 weeks' gestation)				
Brown 2017a Metformin versus glibenclamide **< 37 weeks gestation**	**RR 1.59** (0.59 to 4.29)	508 (3 RCTs)	Very low	Imprecision - wide confidence intervals. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Brown 2017a Glibenclamide versus acarbose **< 37 weeks gestation**	RR not estimable	43 (1 RCT)	Low	Imprecision - one trial with small numbers. Risk of performance bias for not blinding participants and personnel. There were no events reported in either group.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2016a Myo-inositol versus placebo[3] **< 37 weeks gestation**	**RR 1.00** (0.09 to 10.56)	84 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting and four other risk of bias assessments unclear.
Han 2017 Low-moderate GI diet versus moderate-high GI diet **< 37 weeks gestation**	**RR 0.64** (0.22 to 1.85)	146 (2 RCTs)	Low	Risk of performance bias for not blinding participants and personnel and risk of selection bias for no allocation concealment.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories **< 37 weeks gestation**	RR not estimable	84 (1 RCT)	Low	Imprecision - one trial with small numbers. Risk of performance bias for not blinding participants and personnel. There were no events reported in either group
Han 2017 Low-GI diet versus high-fibre moderate-GI diet **< 37 weeks gestation**	**RR 0.96** (0.14 to 6.53)	96 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of detection bias for not blinding outcome assessments and risk of attrition bias for incomplete data.
Han 2017 Diet recommendation + diet-related behavioural advice versus diet recommendation only **< 37 weeks gestation**	**RR 0.51** (0.10 to 2.66)	99 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Soy protein-enriched diet versus no soy protein diet **< 37 weeks gestation**	**RR 2.00** (0.19 to 21.03)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Brown 2017b Lifestyle intervention versus usual care or diet alone **< 37 weeks gestation**	**RR 0.71** (0.53 to 0.96)	1797 (3 RCTs)	Moderate	Risk of performance bias for not blinding participants and personnel in two trials, risk of attrition bias for incomplete data in one trial and risk of reporting bias for selective reporting in one trial.
Brown 2017c Exercise versus control **Weeks not defined**	**RR 0.95** (0.39 to 2.36)	302 (5 RCTs)	Low	Wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel in two trials and risk of attrition bias for incomplete data in one trial.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2012 Intensive management versus routine care **< 37 weeks gestation**	**RR 1.00** (0.26 to 3.82)	138 (2 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of now effect. Risk of performance bias for not blinding participants and personnel.
38.0 Five-minute Apgar < 7				
Brown 2017a Metformin versus glibenclamide	RR not estimable	149 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel. There were no events reported in either group.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 0.56** (0.21 to 1.52)	1030 (1 RCT)	Moderate	Imprecision - one trail with low events rates.
Brown 2017c Exercise versus control	**RR 0.33** (0.01 to 7.65)	343 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of attrition bias for incomplete outcome data and all other risk of bias assessments are unclear.
39.0 Birthweight and z score (included reviews did not report z-scores)				
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo)	**MD -33.0** g (-134.53 to 68.53)	375 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting, no published protocol was found. The population was 93% Hispanic, results may not be generalisable. The trial appears to be registered twice with the same outcomes.
Brown 2017a Metformin versus glibenclamide	**MD -209.13** g (-314.53 to 103.73)	349 (2 RCTs)	Very low	Imprecision - wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding of participants and personnel and risk of reporting bias for selective reporting.
Brown 2017a Glibenclamide versus acarbose	**MD 153.0 g** (-123.52 to 429.52)	43 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2016a Myo-inositol versus placebo[3]	**MD 16.00 g** (-209.72 to 241.72)	73 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect.
Han 2017 Low-moderate GI diet versus moderate-high GI diet	**MD -55.98** g (-201.90 to 89.95)	145 (2 RCTs)	Very low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of selection bias for no allocation concealment.
Han 2017 Energy restricted diet versus no energy restricted diet	**MD -107.00** g (-240.32 to 26.32)	299 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents	**MD -.581.27** g (-790.32 to -372.22)	86 (2 RCT)	Moderate	Imprecision - wide confidence intervals. Unclear risk of bias for four assessments.
Han 2017 Low-carbohydrate diet versus high-carbohydrate diet	**MD 22.00** g (-241.06 to 285.06)	30 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2017 High unsaturated fat diet versus low unsaturated fat diet with matching calories	**MD -138.19** g (-292.59 to 16.21)	111 (2 RCTs)	Low	Imprecision - wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel. Unbalanced groups at baseline for BMI.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet	**MD 0.0** g (-277.18 to 277.18)	92 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of detection bias for not blinding outcome assessments and risk of attrition bias for incomplete outcome data.
Han 2017 Soy protein-enriched diet versus no soy protein diet	**MD -142.60** g (-360.40 to 75.20)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 High-fibre diet versus standard-fibre diet	**MD -94.00** g (-446.71 to 258.71)	22 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 Ethnic specific diet versus standard healthy diet	**MD -370.00** g (-928.87 to 188.87)	20 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**MD -109.64** g (-149.77 to -69.51)	3074 (6 RCT)	Moderate	Risk of performance bias for not blinding participants and personnel in two trials, risk of attrition bias for incomplete data in one trial and risk of reporting bias for selective reporting in four trials.
Brown 2017c Exercise versus control	**MD -61.50** g (-195.21 to 72.20)	192 (6 RCTs)	Very low	Imprecision - with wide confidence intervals crossing the line of no effect. Risk of performance bias for not blinding participants and personnel in two trials and risk of attrition bias for incomplete data in one trial. For most trials unclear risk of bias assessments.
Han 2012 Intensive management versus routine care	**MD -117.33** g (-198.72 to -35.94)	521 (4 RCTs)	Very low	Imprecision - wide confidence intervals. Risk of performance bias for not blinding participants and personnel (four trials), risk of attrition bias for incomplete data (two trials) and reporting bias for selective reporting (1 trial).
Martis 2016a Strict intensity of glycaemic control[2] versus less strict glycaemic control	**MD -0.92** g (-241.97 to 57.97)	171 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
40.0 Head circumference and z score at birth (included reviews did not report z-scores)				
Han 2017 Low-moderate GI diet versus moderate-high GI diet	**MD 0.40** cm (-0.58 to 1.38)	59 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents	**MD -0.90** cm (-1.44 to -0.36)	52 (1 RCT)	Moderate	Imprecision - one trial with small numbers and unclear risk of bias for three bias assessments.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet	**MD -0.20** cm (-0.91 to 0.51)	82 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of detection bias for not blinding outcome assessments and risk of attrition bias for incomplete outcome data.
Han 2017 Soy protein-enriched diet versus no soy protein diet	**MD -0.20** cm (-1.01 to 0.61)	68 (1 RCT)	Very low	Imprecision - one trial small numbers and with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
41.0 Length and z score at birth (included reviews did not report z-scores)				
Han 2017 Low-moderate GI diet versus moderate-high GI diet	**MD -0.50** cm (-1.54 to 0.54)	60 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents	**MD -0.50** cm (-1.59 to 0.59)	52 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Unclear risk of bias for three bias assessments.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet	**MD 0.0** cm (-0.83 to 0.83)	92 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of detection bias for not blinding outcome assessments and risk of attrition bias for incomplete outcome data.
Han 2017 Soy protein-enriched diet versus no soy protein diet	**MD -0.10** cm (-1.07 to 0.87)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and with wide confidence interval crossing the line of no effect. Risk of performance bias for not blinding participants and personnel.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**MD -0.10** cm (-0.37 to 0.17)	700 (1 RCT)	Low	Imprecision - one trial. Risk of attrition bias for incomplete data and risk of reporting bias for selective reporting.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2017c Exercise versus control	**MD -1.70** cm (-3.41 to 0.01)	34 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of attrition bias for incomplete outcome data and unclear risk of bias for all other risk of bias assessments.
42.0 Ponderal index				
Brown 2017a Metformin versus glibenclamide	**MD -0.09** units (-0.17 to -0.01)	200 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet	**MD -0.10** kg/m^3 (-0.03 to 0.23)	60 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel.
Han 2017 DASH[1] diet versus control diet with matching macronutrient contents	**MD -0.37** kg/m^3 (-0.54 to -0.20)	52 (1 RCT)	Moderate	Imprecision - one trial with small numbers and unclear risk of bias for three bias assessments.
Han 2017 Low-GI diet versus high-fibre moderate-GI diet	**MD 0.20** kg/m^3 (-0.79 to 1.19)	92 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of detection bias for not blinding outcome assessments and risk of attrition bias for incomplete outcome data.
Han 2012 Intensive management versus routine care	**MD -0.09** g x 100 m^3 (-0.16 to -0.02)	300 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data.
45.0 Respiratory distress syndrome (RDS)				
Boulvain 2001 Induction of labour versus expectant management	RR not estimable	200 (1 RCT)	Very low	Imprecision - one trial. Risk of bias for all assessments unclear, as not reported in the review. There were no events reported in either group.
Brown 2017a Metformin versus glibenclamide	**RR 0.51** (0.10 to 2.69)	159 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2017a Glibenclamide versus acarbose	RR not estimable	43 (1 RCT)	Low	Imprecision - one trial with small numbers. Risk of performance bias for not blinding participants and personnel. There were no events reported in either group.
Han 2017 Ethnic specific diet versus standard healthy diet	RR not estimable	20 (1 RCT)	Low	Imprecision - one trial with small numbers. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data. There were no events reported in either group.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**average RR 0.79** (0.34 to 1.85)	2195 (4 RCTs)	Moderate	Risk of performance bias for not blinding participants and personnel in two trials and risk of reporting bias for selective reporting in one trial.
Brown 2017c Exercise versus control	RR not estimable	34 (1 RCT)	Very low	Imprecision - one study with small numbers. Risk of attrition bias for incomplete data. Unclear for all other risk of bias assessments. There were no events reported in either group.
46.0 Neonatal jaundice (hyperbilirubinaemia) (as defined in the reviews) (defined in one review only)				
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo)	**RR 1.97** (0.50 to 7.75)	375 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting, no published protocol was found. The population was 93% Hispanic, results may not be generalisable. The trial appears to be registered twice with the same outcomes.
Brown 2017a Metformin versus glibenclamide	**RR 0.68** (0.37 to 1.25)	1205 (2 RCTs)	Moderate	Risk of performance bias for not blinding participants and personnel and risk of reporting bias for selective reporting.
Han 2017 Energy restricted diet versus no energy restricted diet	**RR 0.81** (0.33 to 1.98)	299 (1 RCT)	Low	Imprecision - one trial with wide confidence interval. Risk of performance bias for not blinding participants and personnel.
Han 2017 Soy protein-enriched diet versus no soy protein diet	**RR 0.27** (0.08 to 0.89)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Han 2017 Ethnic specific diet versus standard healthy diet	RR not estimable	20 (1 RCT)	Low	Imprecision - one trial with small numbers. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data. There were no events reported in either group.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**average RR 0.76** (0.50 to 1.16)	2362 (4 RCT's)	Moderate	Risk of performance bias for not blinding of participants and personnel in two trials and risk of attrition bias for incomplete data in one trial.
Brown 2017c Exercise versus control	**RR 0.33** (0.01 to 7.65)	34 (1 RCT)	Very low	Imprecision - one study with small numbers and wide confidence interval. Risk of attrition bias for incomplete data. Unclear for all other risk of bias assessments. There was no event reported in the treatment group and one event reported in the control group.
Han 2012 Intensive management versus routine care. Defined as: **One trial: plasma bilirubin at least 205 µmol/l** **One trial: plasma bilirubin at least 670 µmol/l**	**RR 0.79** (0.24 to 2.60)	426 (2 RCTs)	Low	Imprecision - wide confidence intervals. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data. Heterogeneity: I^2 = 50%.
47.0 Hypocalcaemia (as defined in the reviews) (not defined in the included reviews)				
Han 2017 Energy restricted diet versus no energy restricted diet	**RR 1.36** (1.00 to 1.86)	299 (1 RCT)	Low	Imprecision - one trial with wide confidence intervals. Risk of performance bias for not blinding participants and personnel.
Han 2017 Ethnic specific diet versus standard healthy diet	RR not estimable	20 (1 RCT)	Low	Imprecision - one trial. Risk of performance bias for not blinding participants and personnel and risk of attrition bias for incomplete data. There were no events reported in either group.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 1.38** (1.01 to 1.88)	462 (2 RCTs)	Moderate	Risk of performance bias for not blinding participants and personnel and risk of detection bias for not blinding outcome assessments.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2017c Exercise versus control	RR not estimable	34 (1 RCT)	Very low	Imprecision - one study with small numbers. Risk of attrition bias for incomplete data. Unclear for all other risk of bias assessments. There were no events reported in either group.
48.0 Polycythaemia (as defined in the reviews) (not defined in the review)				
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 0.22** (0.01 to 5.40)	165 (1 RCT)	Low	Imprecision - one trial with wide confidence interval. Risk of performance bias for not blinding participants and personnel. There was event of polycythaemia reported in the control group.

CI: confidence interval; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

***GRADE ratings of evidence**
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1]DASH is an acronym for **D**ietary **A**pproaches to **S**top **H**ypertension
[2]Strict intensity of glycaemic control: pre-prandial 5.0 mmol/L (90 mg/d) and at one-hour post-prandial: 6.7 mmol/L (120 mg/d). Less strict glycaemic control: pre-prandial 5.8 mmol/L (104 mg/d) and at one-hour post-prandial 7.8 mmol/L (140 mg/d)
[3]4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice

Table 2.14: Quality assessment table - Later infant/childhood - secondary outcomes

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
49.0 Weight and z scores (included review reported no z scores)				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Weight at four to five years of age**	**MD -0.30** kg (-1.29 to 0.69)	199 (1 RCT)	Low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of attrition bias as it only reports on 199 children of original trial of 1000 participants.
50.0 Height and z scores (included review reported no z scores)				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Height at four to five years of age**	**MD -0.60** cm (-2.05 to 0.85)	199 (1 RCT)	Low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of attrition bias as it only reports on 199 children of original trial of 1000 participants.
53.1 Impaired glucose tolerance: fasting blood glucose				
Brown 2017b Lifestyle intervention versus usual care or diet alone **At seven to 11 years of age**	**MD 0.10** mmol/L (-0.10 to 0.30)	68 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting.
53.2 Impaired glucose tolerance: post-prandial blood glucose				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Two hours post-prandial at seven to 11 years of age**	**MD 0.00** mmol/L (-0.48 to 0.48)	68 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting.
54.0 Dyslipidaemia or metabolic syndrome (as defined in the reviews)				
Brown 2017b Lifestyle intervention versus usual care or diet alone **Total cholesterol at seven to 11 years of age**	**MD -0.20** mg/dL (-0.55 to 0.15)	68 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting.
Brown 2017b Lifestyle intervention versus usual care or diet alone **LDL[1] cholesterol at seven to 11 years of age**	**MD -0.12** mg/dL (-0.50 to 0.26)	68 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting.
Brown 2017b Lifestyle intervention versus usual care or diet alone **HDL[2] cholesterol at seven to 11 years of age**	**MD 0.10** mg/dL (-0.05 to 0.25)	68 (1 RCT)	Low	Imprecision - one trial with small numbers and wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting.

CI: confidence interval; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

***GRADE ratings of evidence**
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1]LDL is an acronym for **L**ow **D**ensity **L**ipoprotein cholesterol
[2]HDL is an acronym for **H**igh-**D**ensity **L**ipoprotein cholesterol

Table 2.15: Quality assessment table - Health service use - secondary outcomes

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
57.1 Visits with dietitian				
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 9.24** (7.12 to 12.01)	1000 (1 RCT)	Moderate	Imprecision - one trial with wide confidence interval.
57.2 Visits with diabetes educator				
Brown 2017b Lifestyle intervention versus usual care or diet alone	**RR 8.55** (6.67 to 10.96)	1000 (1 RCT)	Moderate	Imprecision - one trial with wide confidence interval.
57.3. Visits with obstetrician				
Brown 2017b Lifestyle intervention versus usual care or diet alone	**MD 0.20** visits (-0.21 to 0.61)	700 (1 RCT)	Low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of attrition bias for incomplete outcome data and risk of reporting bias for selective reporting.
57.4 Visits with healthcare provider (not specified)				
Brown 2017b Lifestyle intervention versus usual care or diet alone	**MD 0.10** visits (-1.58 to 1.78)	197 (1 RCT)	Low	Imprecision - one trial with wide confidence interval crossing the line of no effect. Risk of reporting bias for selective reporting and risk of performance bias for not blinding participants and personnel.
58.0 Admission to neonatal intensive care unit/nursery				
Han 2017 Soy protein-enriched diet versus no soy protein diet Admission was defined as "hypoxia, low-risk Apgar scores 6-7 (at 5 or 15 min of age), high-risk Apgar scores at 1 minute 0-5 and at 5 or 15 minutes less than 6, hyperbilirubinaemia, birth weight less than 2500 g, and/or gestational age less than 32 weeks, sepsis, pneumonia, or meningitis, hypoglycaemia (blood glucose < 1.7mmol/L)"	**RR 0.14** (0.02 to 1.10)	68 (1 RCT)	Very low	Imprecision - one trial with small numbers and wide confidence interval. Risk of performance bias for not blinding participants and personnel.

Intervention and comparison and outcome	Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments from overview review authors
Brown 2017a Oral antidiabetic agents versus placebo (Glibenclamide versus placebo)	**RR 1.16** (0.53 to 2.53)	375 (1 RCT)	Very low	Imprecision - one trial with wide confidence interval. Risk of reporting bias for selective reporting.
Brown 2017a Metformin versus glibenclamide	**RR 1.52** (0.65 to 3.56)	349 (2 RCTs)	Low	Imprecision - wide confidence interval. Risk of reporting bias for selective reporting and risk of performance bias not blinding participants and personnel.
Han 2012 Intensive management versus routine care	**RR 0.64** (0.29 to 1.45)	426 (2 RCTs)	Moderate	Risk of attrition bias for incomplete outcome data in one trial and risk of performance bias for not blinding participants and personnel in both trials.
Brown 2017b Lifestyle intervention versus usual care or diet alone	**average RR 0.91** (0.59 to 1.40)	2030 (3 RCTs)	Low	Heterogeneity: I^2 = 80%. Risk of reporting bias for selective reporting in one trial and risk of performance bias for not blinding participants and personnel in one trial.

CI: confidence interval; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

***GRADE ratings of evidence**
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

AMSTAR assessment

Using the AMSTAR tool, seven included reviews assessed were of high methodological quality scoring between 9 and 11 points (Brown 2017a; Brown 2017b; Brown 2017c; Brown 2016a; Han 2017; Han 2012; Martis 2016a). One review assessed was of moderate methodological quality scoring 7 points due to no recent up-date and lack of information about the methodological quality assessment (Boulvain 2001) (Table 2.16).

The assessment for each of the 11 items of the AMSTAR tool are as follows:

1. All reviews provided a priori design.
2. All reviews reported duplicate study selection and data extraction.
3. All reviews performed a comprehensive literature search.
4. All reviews included searches of grey literature.
5. All reviews provided a list of included and excluded studies.
6. All reviews described the characteristics of the included studies.
7. All reviews assessed and documented the scientific quality of the included studies.
8. Seven reviews assessed the scientific quality of the included studies appropriately in formulating conclusion. One review did not assess the scientific quality.
9. Six reviews combined the findings of studies using appropriate methods. For two reviews this was not applicable as both included only one RCT.
10. Four reviews assessed the likelihood of publication bias. The other four reviews did not mention that publication bias could not be assessed because there were fewer than 10 included studies but included test values or funnel plots.
11. Six reviews clearly reported conflict of interest.

Table 2.16: AMSTAR assessments for included reviews

Review ID	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
AMSTAR Domains **Answer code: √ = Yes; x = No; ? = Unclear;** **NA = Not applicable**								
1. Was an a priori design provided?	√	√	√	√	√	√	√	√
2. Was there duplicate study selection and data extraction?	√	√	√	√	√	√	√	√
3. Was a comprehensive literature search performed?	√	√	√	√	√	√	√	√
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	√	√	√	√	√	√	√	√
5. Was a list of studies (included and excluded) provided?	√	√	√	√	√	√	√	√
6. Were the characteristics of the included studies provided?	√	√	√	√	√	√	√	√
7. Was the scientific quality of the included studies assessed and documented?	√	√	√	√	√	√	√	√
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	x	√	√	√	√	√	√	√
9. Were the methods used to combine the findings of studies appropriate?	NA	√	√	√	√	√	√	NA
10. Was the likelihood of publication bias assessed? *	x	√	√	√	x	√	x	x
11. Was the conflict of interest included?	x	√	√	√	√	√	x	√
Total Score (out of 11): **Score interpretation: √** **8-11 = High quality** **4-7 = Moderate quality** **≤3 = Low quality**	**7/11 Moderate quality**	**11/11 High quality**	**11/11 High quality**	**11/11 High quality**	**10/11 High quality**	**11/11 High quality**	**9/11 High quality**	**9/11 High quality**

*We judged publication bias assessed as a 'yes' when a funnel plot and at least 10 studies were included in the review

ROBIS assessment

Overall the risk of bias for the included reviews using the ROBIS tool were judged as low risk for seven reviews (Brown 2017a; Brown 2017b; Brown 2017c; Brown 2016a; Han 2017; Han 2012; Martis 2016a) and as unclear risk for one review due to lack of evidence to minimise error in risk of bias assessment in that review. (Boulvain 2001) (Table 2.17).

The assessment for each of the four domains of the ROBIS tool are as follows:

Domain 1: All reviews were considered of low concern for specification of study eligibility criteria.

Domain 2: All reviews were considered of low concern regarding methods used to identify and/or select studies.

Domain 3: Seven reviews were considered of low concern regarding methods used to collect data and appraise studies. One study was of unclear concern as there was no evidence of risk of bias assessment.

Domain 4: All reviews were considered of low concern regarding synthesis and findings, although one study did not include a funnel plot or sensitivity analysis.

Table 2.17: ROBIS assessment for included reviews

Review ID	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
ROBIS DOMAINS **Answer Code: √ = Yes; x = No; ? = unclear**								
Domain 1: Study eligibility criteria								
Did the review adhere to pre-defined objectives and eligibility criteria?	√	√	√	√	√	√	√	√
Were the eligibility criteria appropriate for the review question?	√	√	√	√	√	√	√	√
Were eligibility criteria unambiguous?	√	√	√	√	√	√	√	√
Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	√	√	√	√	√	√	√	√
Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	√	√	√	√	√	√	√	√
Concerns regarding specification of study eligibility criteria **LOW, HIGH, UNCLEAR**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
Domain 2: Identification and selection of studies								
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	√	√	√	√	√	√	√	√
Were methods additional to database searching used to identify relevant reports?	√	√	√	√	√	√	√	√
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	√	√	√	√	√	√	√	√
Were restrictions based on date, publication format, or language appropriate?	√	√	√	√	√	√	√	√
Were efforts made to minimise error in selection of studies?	√	√	√	√	√	√	√	√
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
Domain 3: Data collection and study appraisal								
Were efforts made to minimise error in data collection?	√	√	√	√	√	√	√	√

Review ID	Boulvain 2001	Brown 2017a	Brown 2017b	Brown 2017c	Brown 2016a	Han 2017	Han 2012	Martis 2016a
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	√	√	√	√	√	√	√	√
Were all relevant study results collected for use in the synthesis?	√	√	√	√	√	√	√	√
Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	x	√	√	√	√	√	√	√
Were efforts made to minimise error in risk of bias assessment?	x	√	√	√	√	√	√	√
Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	**Unclear**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
Domain 4: Synthesis and findings								
Did the synthesis include all studies that it should?	√	√	√	√	√	√	√	√
Were all pre-defined analyses reported or departures explained?	√	√	√	√	√	√	√	√
Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	√	√	√	√	√	√	√	√
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	√	√	√	√	√	√	√	√
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	x	√	√	√	√	√	√	√
Were biases in primary studies minimal or addressed in the synthesis?	√	√	√	√	√	√	√	√
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
Risk of bias in the review								
Did the interpretation of findings address all concerns identified in Domains 1-4?	x	√	√	√	√	√	√	√
Was the relevance of identified studies to the review's research question appropriately considered?	√	√	√	√	√	√	√	√
Did the reviewers avoid emphasising results on the basis of their statistical significance?	√	√	√	√	√	√	√	√
Overall Risk of Bias (According to Whiting 2016)	**Unclear Risk**	**Low Risk**	**Low Risk**	**Low Risk**	**Low Risk**	**Low Risk**	**Low Risk**	**Low Risk**

Effects of interventions

We summarised the results of the included reviews by categorising their findings using the following framework organised by the overview review outcomes:

- Effective interventions: indicating that the review found high-quality evidence of effectiveness for an intervention.
- Promising interventions (more evidence needed): indicating that the review found moderate-quality evidence of effectiveness for an intervention, but more evidence is needed.
- Probably no difference between interventions: direction of effect suggests benefit/harm or ineffective, 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, more evidence needed.

For further details see *Characteristics of included reviews* (Table 2.5). For the pre-specified GRADE outcomes see *Summary of findings tables* for maternal (Table 2.8), child (as neonate, child, adult) (Table 2.9) and health service use (Table 2.10).

Additional quality assessments for non-GRADE *maternal secondary outcomes*; *maternal long term secondary outcomes*; *fetal/neonatal secondary outcomes*; *later infant/childhood secondary outcomes and health service use* have been summarised in Table 2.11, Table 2.12, Table 2.13, Table 2.14, and Table 2.15 respectively.

For the assessment summary of interventions for *all* overview review outcomes see Table 2.18 for primary outcomes and Table 2.19 for secondary outcomes.

Table 2.18: Summary of main results - all primary outcomes (maternal and neonatal)

Primary Outcomes – Maternal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
1.1 Any hypertensive disorders of pregnancy, not defined		Metformin versus glibenclamide **(Brown 2017a)**	Glibenclamide versus placebo **(Brown 2017a)**
1.2 Pregnancy induced hypertension		Metformin versus glibenclamide **(Brown 2017a)**	Glibenclamide versus placebo **(Brown 2017a)**
			Low carbohydrate diet versus high carbohydrate diet **(Han 2017)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)**
			Ethnic specific diet versus standard healthy diet **(Han 2017)**
1.3 Severe hypertension or pre-eclampsia			Glibenclamide versus placebo **(Brown 2017a)**
			Low-moderate GI diet versus moderate-high GI diet **(Han 2017)**
1.4 Pre-eclampsia (not defined)		DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)**	Metformin versus glibenclamide **(Brown 2017a)**
			Energy restricted diet versus no energy restricted diet **(Han 2017)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)**
			Soy protein-enriched diet versus no soy protein diet **(Han 2017)**
			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
			Exercise versus control **(Brown 2017c)**
			Intensive management versus routine care **(Han 2012)**
1.5 Eclampsia (not defined)			Low-moderate GI diet versus moderate-high GI die **(Han 2017)**

Primary Outcomes – Maternal		Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**		**Low or Very Low-Quality Evidence**
2.0 Caesarean section		DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)**		Induction of labour versus expectant management **(Boulvain 2001)**
		Exercise versus control **(Brown 2017c)**		Glibenclamide versus placebo **(Brown 2017a)**
				Metformin versus glibenclamide **(Brown 2017a)**
				Glibenclamide versus acarbose **(Brown 2017a)**
				Low-moderate GI diet versus moderate-high GI diet **(Han 2017)**
				Energy restricted diet versus no energy restricted diet **(Han 2017)**
				Low carbohydrate diet versus high-carbohydrate diet **(Han 2017)**
				High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)**
				Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)**
				Diet recommendation + diet-related behavioural advice versus diet recommendation only **(Han 2017)**
				Soy protein-enriched diet versus no soy protein diet (**Han 2017)**
				Ethnic specific diet versus standard healthy diet **(Han 2017)**
				Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
				Intensive management versus routine care **(Han 2012)**
				Strict intensity of glycaemic control[2] versus less strict glycaemic control **(Martis 2016a)**
3.1 OGTT (Oral Glucose Tolerance Test) for diagnosis of type 2 diabetes				High unsaturated fat diet versus low unsaturated fat diet with matching calories at one to two weeks post-partum **(Han 2017)**

Primary Outcomes – Maternal		Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**		**Low or Very Low-Quality Evidence**
				Low-GI diet versus high fibre moderate-GI diet at three months post-partum **(Han 2017)**
				High unsaturated fat diet versus low unsaturated fat diet with matching calories at four to 13 months post-partum **(Han 2017)**
				Lifestyle intervention versus usual care or diet alone (test and time frame not defined **(Brown 2017b)**

Primary Outcomes - Neonatal		Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**		**Low or Very Low-Quality Evidence**
4.0 Perinatal (fetal and neonatal death) and later infant mortality All included reviews reported on perinatal mortality only				Induction of labour versus expectant management **(Boulvain 2001)**
				Metformin versus glibenclamide **(Brown 2017a)**
				Glibenclamide versus acarbose **(Brown 2017a)**
				Energy restricted diet versus no energy restricted diet **(Han 2017)**
				Low carbohydrate diet versus high-carbohydrate diet **(Han 2017)**
				Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
				Exercise versus control **(Brown 2017c)**
5.0 Large-for-gestational age (LGA) (defined as > 90th percentile in all included reviews)		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**		Induction of labour versus expectant management **(Boulvain 2001)**
				Glibenclamide versus placebo **(Brown 2017a)**
				Metformin versus glibenclamide (**Brown 2017a)**
				Glibenclamide versus acarbose **(Brown 2017a)**

Primary Outcomes - Neonatal		Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**		**Low or Very Low-Quality Evidence**
				4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice **(Brown 2016a)** Low-moderate GI diet versus moderate-high GI diet **(Han 2017)** Energy restricted diet versus no energy restricted diet **(Han 2017)** Low carbohydrate diet versus high-carbohydrate diet **(Han 2017)** High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)** Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)** Diet recommendation + diet-related behavioural advice versus diet recommendation only **(Han 2017)** Ethnic specific diet versus standard healthy diet **(Han 2017)** Intensive management versus routine care **(Han 2012)**
6.0 Death or serious morbidity composite (as defined in reviews, e.g. perinatal or infant death, shoulder dystocia, bone fracture or nerve palsy)		Exercise versus control **(Brown 2017c)**		Metformin versus glibenclamide. The morbidity composite included hypoglycaemia, hyperbilirubinaemia, macrosomia, respiratory illness, birth injury, stillbirth or neonatal death. **(Brown 2017a)** Ethnic specific diet versus standard healthy diet. The morbidity composite included hypoglycaemia, neonatal asphyxia, respiratory distress syndrome, hyperbilirubinaemia and hypocalcaemia **(Han 2017)** Lifestyle intervention versus usual care or diet alone. The death or serious morbidity composite included death, shoulder dystocia, bone fracture and nerve palsy in one trial and in the other trial included stillbirth, neonatal death, hypoglycaemia, hyperbilirubinaemia, elevated cord-blood C-peptide and birth trauma **(Brown 2017b)**

Table 2.19: Summary of main results - all secondary outcomes (maternal, neonatal, later infant/childhood/adult and health service use)

Secondary Outcomes - Maternal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
8.0 Use of additional pharmacotherapy		DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)**	Glibenclamide versus placebo (insulin**) (Brown 2017a)**
		Lifestyle intervention versus usual care or diet alone (oral antidiabetic agents) **(Brown 2017b)**	Acarbose versus placebo (insulin) **(Brown 2017a)**
			Metformin versus glibenclamide (insulin) **(Brown 2017a)**
			Glibenclamide versus acarbose (insulin) **(Brown 2017a)**
			4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice (insulin) **(Brown 2016a)**
			Low-moderate GI diet versus moderate-high GI diet (not defined) **(Han 2017)**
			Energy restricted diet versus no energy restricted diet (insulin) **(Han 2017)**
			Low carbohydrate diet versus high-carbohydrate diet (not defined) **(Han 2017)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories (not defined) **(Han 2017)**
			Low-GI diet versus high-fibre moderate-GI diet (not defined) **(Han 2017)**
			Diet recommendation + diet-related behavioural advice versus diet recommendation only (not defined**) (Han 2017)**
			Soy protein-enriched diet versus no soy protein diet (not defined) **(Han 2017)**
			High-fibre diet versus standard-fibre diet (not defined) **(Han 2017)**
			Ethnic specific diet versus standard healthy diet (not defined) **(Han 2017)**
			Lifestyle intervention versus usual care or diet alone (insulin) **(Brown 2017b)**
			Exercise versus control **(Brown 2017c)**
			Intensive management versus routine care (insulin or oral hypoglycaemics) **(Han 2012)**

Secondary Outcomes - Maternal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
			Strict intensity of glycaemic control[2] versus less strict glycaemic control (insulin) **(Martis 2016a)**
9.0 Maternal hypoglycaemia (as defined in the reviews)			Metformin versus glibenclamide maternal hypoglycaemia as < 3.3 mmol/L (60 mg/dL) (one trial) **(Brown 2017a)** Glibenclamide versus acarbose (not defined) **(Brown 2017a)** High-fibre diet versus standard-fibre diet (not defined) **(Han 2017)** Lifestyle intervention versus usual care or diet alone (not defined) **(Brown 2017b)** Exercise versus control **(Brown 2017c)**
10.1 Glycaemic control: timing not defined			Low-GI diet versus high-fibre moderate-GI diet (not defined) **(Han 2017)**
10.2 Glycaemic control *during* the treatment: pre-prandial/fasting			Energy restricted diet versus no energy restricted diet (during not defined) **(Han 2017)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories (at 38 weeks gestation) **(Han 2017)**
10.3 Glycaemic control *during* the treatment: post-prandial			Energy restricted diet versus no energy restricted diet (at one hour) **(Han 2017)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories (no post-prandial time given) (at 38 weeks gestation) **(Han 2017)**
10.4 Glycaemic control *during* treatment: HbA1c			Metformin versus glibenclamide **(Brown 2017a)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories (at 38 weeks gestation) **(Han 2017)**
10.5 Glycaemic control *during* the treatment: 24 hours mean plasma glucose			Energy restricted diet versus no energy restricted diet **(Han 2017)**
10.6 Glycaemic control at the *end* of treatment: Fasting		4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice (with OGTT) **(Brown 2016a)**	Glibenclamide versus placebo (taken at the last three antenatal visits) **(Brown 2017a)**

Secondary Outcomes - Maternal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
		DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)**	Metformin versus glibenclamide **(Brown 2017a)**
			Low-moderate GI diet versus moderate-high GI diet **(Han 2017)**
			Energy restricted diet versus no energy restricted diet **(Han 2017)**
			Low carbohydrate diet versus high-carbohydrate diet **(Han 2017)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)**
			Diet recommendation + diet-related behavioural advice versus diet recommendation only **(Han 2017)**
			Soy protein-enriched diet versus no soy protein diet **(Han 2017)**
			Exercise versus control **(Brown 2017c)**
10.7 Glycaemic control at the *end* of treatment: One hour post-prandial		4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice (with OGTT) **(Brown 2016a)**	Energy restricted diet versus no energy restricted diet **(Han 2017)**
			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
10.8 Glycaemic control at the *end* of treatment: Two hours post-prandial			Metformin versus glibenclamide (After DINNER where specified) **(Brown 2017a)**
			4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice (with OGTT) **(Brown 2016a)**
			Low-moderate GI diet versus moderate-high GI diet **(Han 2017)**
			Low carbohydrate diet versus high-carbohydrate diet (after BREAKFAST) **(Han 2017)**
			Low carbohydrate diet versus high-carbohydrate diet (after LUNCH) **(Han 2017)**
			Low carbohydrate diet versus high-carbohydrate diet (after DINNER) **(Han 2017)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)**

Secondary Outcomes - Maternal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
10.9 Glycaemic control at the *end* of treatment: Post-prandial timing not defined		Exercise versus control **(Brown 2017c)**	Diet recommendation + diet-related behavioural advice versus diet recommendation only **(Han 2017)** Exercise versus control (with OGTT) **(Brown 2017c)**
10.10 Glycaemic control at the *end* of treatment: mean plasma glucose			Energy restricted diet versus no energy restricted diet (24 hours mean) **(Han 2017)** Exercise versus control **(Brown 2017c)**
10.11 Glycaemic control at the *end* of treatment: HbA1c	Exercise versus control **(Brown 2017c)**	DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)**	Low-moderate GI diet versus moderate-high GI diet **(Han 2017)** Diet recommendation + diet-related behavioural advice versus diet recommendation only **(Han 2017)** Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
10.12 Glycaemic control *during/at the end* of treatment: Fasting			Energy restricted diet versus no energy restricted diet **(Han 2017)** Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
10.13 Glycaemic control *during/at the end* of treatment: Mean plasma glucose			Energy restricted diet versus no energy restricted diet **(Han 2017)** High-fibre diet versus standard-fibre diet **(Han 2017)**
10.14 Glycaemic control *during/at the end* of treatment: Mean HbA1c			Energy restricted diet versus no energy restricted diet **(Han 2017)**
11.0 Weight gain in pregnancy		DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)**	Glibenclamide versus placebo **(Brown 2017a)**
		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Metformin versus glibenclamide **(Brown 2017a)**
			Glibenclamide versus acarbose **(Brown 2017a)**

Secondary Outcomes - Maternal		Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**		**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
				4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice **(Brown 2016a)**
				Low-moderate GI diet versus moderate-high GI diet **(Han 2017)**
				Energy restricted diet versus no energy restricted diet **(Han 2017)**
				Low-carbohydrate diet versus high-carbohydrate diet **(Han 2017)**
				High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)**
				Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)**
				Diet recommendation + diet-related behavioural advice versus diet recommendation only **(Han 2017)**
				Soy protein-enriched diet versus no soy protein diet **(Han 2017)**
				High-fibre diet versus standard-fibre diet **(Han 2017)**
				Ethnic specific diet versus standard healthy diet **(Han 2017)**
				Exercise versus control **(Brown 2017c)**
				Intensive management versus routine care **(Han 2012)**
12.0 Other measures of weight gain in pregnancy (not pre-specified for this overview) **- BMI during the pregnancy** **- BMI at the end of the Pregnancy** **- Excessive weight gain in pregnancy**			4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice (BMI during) **(Brown 2016a)**	Diet recommendation + diet-related behavioural advice versus diet recommendation only (BMI at end) **(Han 2017)**
			DASH[1] diet versus control diet with matching macronutrient contents (BMI at end) **(Han 2017)**	Soy protein-enriched diet versus no soy protein diet (BMI at end) **(Han 2017)**
				Exercise versus control (excessive weight gain in pregnancy) **(Brown 2017c)**
13.0 Adherence to the intervention				Low-carbohydrate diet versus high-carbohydrate diet **(Han 2017)**
				Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)**
				Ethnic specific diet versus standard healthy diet **(Han 2017)**
				Exercise versus control **(Brown 2017c)**

Secondary Outcomes - Maternal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
14.0 Induction of labour	Lifestyle intervention versus usual care or diet alone (Brown 2017b)		Glibenclamide versus placebo **(Brown 2017a)** Metformin versus glibenclamide **(Brown 2017a)** Low-moderate GI diet versus moderate-high GI diet **(Han 2017)** Energy restricted diet versus no energy restricted diet **(Han 2017)** Exercise versus control **(Brown 2017c)** Intensive management versus routine care **(Han 2012)**
15. Placental abruption			DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)** High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)**
16.0 Postpartum haemorrhage (as defined in the reviews)			Low-moderate GI diet versus moderate-high GI diet (PPH not defined) **(Han 2017)** Lifestyle intervention versus usual care or diet alone (PPH not defined) **(Brown 2017b)**
17.0 Postpartum infection		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Low-moderate GI diet versus moderate-high GI diet **(Han 2017)**
18.0 Perineal trauma/tearing		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Glibenclamide versus placebo **(Brown 2017a)** Metformin versus glibenclamide **(Brown 2017a)**
19.1 Breastfeeding at discharge		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	
19.1.2 Breastfeeding at six weeks postpartum			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
19.1.3 Breastfeeding at six months post-partum or longer			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
20.0 Maternal mortality			Exercise versus control **(Brown 2017c)**
21.1 Sense of well-being and quality of life *during* treatment: Overall physical component			Lifestyle intervention versus usual care or diet alone (SF-36) **(Brown 2017b)**
21.2 Sense of well-being and quality of life during treatment: Overall mental component			Lifestyle intervention versus usual care or diet alone (SF-36) **(Brown 2017b)**

Secondary Outcomes - Maternal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
21.3 Sense of well-being and quality of life during treatment: Anxiety		Lifestyle intervention versus usual care or diet alone (SF-36) **(Brown 2017b)**	
21.4 Sense of well-being and quality of life at three months post-partum: Overall physical component			Lifestyle intervention versus usual care or diet alone (SF-36) **(Brown 2017b)**
21.5 Sense of well-being and quality of life at three months post-partum: Overall mental component			Lifestyle intervention versus usual care or diet alone (SF-36) **(Brown 2017b)**
21.6 Sense of well-being and quality of life at three months post-partum: Anxiety			Lifestyle intervention versus usual care or diet alone (SF-36) **(Brown 2017b)**
22.0 Women's view of the intervention			Exercise versus control **(Brown 2017c)**
23.1 Relevant biomarker changes: Homeostasis Model Assessment Insulin Resistance (HOMA-IR) and HOMA2-IR		DASH[1] diet versus control diet with matching macronutrient contents (HOMA-IR at end) **(Han 2017)**	Low-GI diet versus high-fibre moderate-GI diet (HOMA2-IR at end) **(Han 2017)** Low-GI diet versus high-fibre moderate-GI diet (HOMA2-IR at 3 months) **(Han 2017)** Diet recommendation + diet-related behavioural advice versus diet recommendation only (HOMA-IR at end) **(Han 2017)** Soy protein-enriched diet versus no soy protein diet (HOMA-IR at end) **(Han 2017)**
23.2 Relevant biomarker changes: Quantitative Insulin Sensitivity Check Index (QUICKI)			Soy protein-enriched diet versus no soy protein diet (QUICKI at the end of the intervention) **(Han 2017)**
23.3 Relevant biomarker changes: Fasting plasma insulin during the intervention			Energy restricted diet versus no energy restricted diet **(Han 2017)** High unsaturated fat diet group compared to low unsaturated fat diet with matching calories (at 38 weeks gestation) **(Han 2017)**

Secondary Outcomes - Maternal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
23.4 Relevant biomarker changes: Fasting plasma insulin at end of treatment			Energy restricted diet versus no energy restricted diet **(Han 2017)**
			DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)**
			Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)**
			Diet recommendation + diet-related behavioural advice versus diet recommendation only **(Han 2017)**
			Soy protein-enriched diet versus no soy protein diet **(Han 2017)**

Secondary Outcomes – Maternal long-term	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
25.0 Postnatal depression			Lifestyle intervention versus usual care or diet alone (defined as Edinburgh Postnatal Depression Score (EPDS) >12) **(Brown 2017b)**
26.0 Body Mass Index (BMI)			Low-GI diet versus high-fibre moderate-GI diet (BMI at 3 months) **(Han 2017)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories (at 5 to 9 months) **(Han 2017)**
27.0 Postnatal weight retention or return to pre-pregnancy weight	Exercise versus control (timing not defined) **(Brown 2017c)**		Lifestyle intervention versus usual care or diet alone (at 6 weeks post-partum) **(Brown 2017b)**
			Low-GI diet versus high-fibre moderate-GI diet (at 3 months post-partum) **(Han 2017)**
			Lifestyle intervention versus usual care or diet alone (at 7 months post-partum) **(Brown 2017b)**
			Lifestyle intervention versus usual care or diet alone (at 12 months post-partum) **(Brown 2017b)**
28.0 Impaired glucose tolerance			Lifestyle intervention versus usual care or diet alone (test and timing not defined) **(Brown 2017b)**

Secondary Outcomes – Maternal long-term	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories (borderline OGTT at one to two weeks post-partum) **(Han 2017)** Low-GI diet versus high-fibre moderate-GI diet (at three months post-partum, measure not defined) **(Han 2017)** Lifestyle intervention versus usual care or diet alone (fasting plasma glucose at three months post-partum) **(Brown 2017b)** Lifestyle intervention versus usual care or diet alone (fasting blood glucose concentration at 6 months post-partum) **(Brown 2017b)** High unsaturated fat diet versus low unsaturated fat diet with matching calories (borderline OGTT at four to 13 months post-partum) **(Han 2017)**
29.0 Cardiovascular health (as defined in the reviews including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)			Lifestyle intervention versus usual care or diet alone (metabolic syndrome) **(Brown 2017b)**

Secondary Outcomes - Fetal/neonatal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
31.0 Stillbirth			Glibenclamide versus placebo **(Brown 2017a)** Metformin versus glibenclamide **(Brown 2017a)** Energy restricted diet versus no energy restricted diet **(Han 2017)** Low-carbohydrate diet versus high-carbohydrate diet **(Han 2017)** Lifestyle intervention versus usual care or diet alone **(Brown 2017b)** Exercise versus control **(Brown 2017c)**
32.0 Neonatal death			Glibenclamide versus placebo **(Brown 2017a)** Energy restricted diet versus no energy restricted diet **(Han 2017)**

Secondary Outcomes - Fetal/neonatal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
33.0 Macrosomia (> 4000 g; or as defined in the reviews)		Exercise versus control (not defined) **(Brown 2017c)**	Induction of labour versus expectant management (> 4000 g) **(Boulvain 2001)**
		Intensive management versus routine care (≥ 4000 g) **(Han 2012)**	Glibenclamide versus placebo (≥ 4000 g) **(Brown 2017a)**
			Metformin versus glibenclamide (≥ 4000 g (1 trial) (≥ 3700 g (1 trial) **(Brown 2017a)**
			Glibenclamide versus acarbose (> 4000 g) **(Brown 2017a)**
			Low-moderate GI diet versus moderate-high GI diet (> 4000 g) **(Han 2017)**
			Energy restricted diet versus no energy restricted diet (> 4000 g) **(Han 2017)**
			Energy restricted diet versus no energy restricted diet (> 4500 g) **(Han 2017)**
			DASH[1] diet versus control diet with matching macronutrient contents (≥ 4000 g) **(Han 2017)**
			Low-carbohydrate diet versus high-carbohydrate diet (> 4000 g) **(Han 2017)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories (> 4000 g) **(Han 2017)**
			Low-GI diet versus high-fibre moderate-GI diet (> 4000 g) **(Han 2017)**
			Soy protein-enriched diet versus no soy protein diet (> 4000 g) **(Han 2017)**
			Ethnic specific diet versus standard healthy diet (> 4000 g) **(Han 2017)**
			Lifestyle intervention versus usual care or diet alone (> 4 kg (5 trials) (≥ 4 kg (2 trials) **(Han 2017)**
			Strict intensity of glycaemic control[2] versus less strict glycaemic control (> 4000 g) **(Martis 2016a)**

Secondary Outcomes - Fetal/neonatal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
34.0 Small-for-gestational age (SGA) (not defined in the reviews)		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Glibenclamide versus placebo **(Brown 2017a)**
			Glibenclamide versus acarbose **(Brown 2017a)**
			Low-moderate GI diet versus moderate-high GI diet **(Han 2017)**
			Low-carbohydrate diet versus high-carbohydrate diet **(Han 2017)**
			Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)**
			Ethnic specific diet versus standard healthy diet **(Han 2017)**
			Intensive management versus routine care **(Han 2012)**
			Strict intensity of glycaemic control versus less strict glycaemic control **(Martis 2016a)**
35.1 Birth trauma not defined			Metformin versus glibenclamide **(Brown 2017a)**
			Glibenclamide versus acarbose **(Brown 2017a)**
			Lifestyle intervention versus usual care or diet alone **(Brown 2017a)**
35.2 Birth trauma: Shoulder dystocia			Induction of labour versus expectant management **(Boulvain 2001)**
			Glibenclamide versus placebo **(Brown 2017a)**
			Metformin versus glibenclamide **(Brown 2017a)**
			Energy restricted diet versus no energy restricted diet **(Han 2017)**
			Intensive management versus routine care **(Han 2012)**
			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
35.3 Birth trauma: Bone fracture			Induction of labour versus expectant management **(Boulvain 2001)**
			Glibenclamide versus placebo **(Brown 2017a)**
			Energy restricted diet versus no energy restricted diet **(Han 2012)**
			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**

Secondary Outcomes - Fetal/neonatal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
35.4 Birth trauma: Nerve palsy (brachial plexus)			Induction of labour versus expectant management **(Boulvain 2001)** Glibenclamide versus placebo **(Brown 2017a)** Energy restricted diet versus no energy restricted diet **(Han 2012)** Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
36.0 Gestational age at birth		4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice **(Brown 2016a)** Energy restricted diet versus no energy restricted diet **(Han 2017)**	Glibenclamide versus placebo **(Brown 2017a)** Metformin versus glibenclamide **(Brown 2017a)** Glibenclamide versus acarbose **(Brown 2017a)** Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)** DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)** Low-carbohydrate diet versus high-carbohydrate diet **(Han 2017)** High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)** Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)** Soy protein-enriched diet versus no soy protein diet **(Han 2017)** High-fibre diet versus standard-fibre diet **(Han 2017)** Ethnic specific diet versus standard healthy diet **(Han 2017)** Lifestyle intervention versus usual care or diet alone **(Brown 2017b)** Exercise versus control **(Brown 2017c)** Intensive management versus routine **care (Han 2012)**

Secondary Outcomes - Fetal/neonatal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
			Strict intensity of glycaemic control[2] versus less strict glycaemic control **(Martis 2016a)**
37.0 Preterm birth (< 37 weeks' gestation and < 32 weeks' gestation)		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Metformin versus glibenclamide **(Brown 2017a)**
			Glibenclamide versus acarbose **(Brown 2017a)**
			4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice **(Brown 2016a)**
			Low-moderate GI diet versus moderate-high GI diet **(Han 2017)**
			High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)**
			Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)**
			Diet recommendation + diet-related behavioural advice versus diet recommendation only **(Han 2017)**
			Soy protein-enriched diet versus no soy protein diet **(Han 2017)**
			Exercise versus control **(Brown 2017c)**
			Intensive management versus routine care **(Han 2012)**
38.0 Five-minute Apgar < 7		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Metformin versus glibenclamide **(Brown 2017a)**
			Exercise versus control **(Brown 2017c)**
39.0 Birthweight and z score (None of the included reviews reported data for birthweight z scores)		DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)**	Glibenclamide versus placebo **(Brown 2017b)**
		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Metformin versus glibenclamide **(Brown 2017a)**
			Glibenclamide versus acarbose **(Brown 2017a)**

Secondary Outcomes - Fetal/neonatal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
			4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice **(Brown 2016a)** Low-moderate GI diet versus moderate-high GI diet **(Han 2017)** Energy restricted diet versus no energy restricted diet **(Han 2017)** Low-carbohydrate diet versus high-carbohydrate diet **(Han 2017)** High unsaturated fat diet versus low unsaturated fat diet with matching calories **(Han 2017)** Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)** Soy protein-enriched diet versus no soy protein diet **(Han 2017)** High-fibre diet versus standard-fibre diet **(Han 2017)** Ethnic specific diet versus standard healthy diet **(Han 2017)** Exercise versus control **(Brown 2017c)** Intensive management versus routine care **(Han 2012)** Strict intensity of glycaemic control[2] versus less strict glycaemic control **(Martis 2016a)**
40.0 Head circumference and z score **(The included review did not reported data for head circumference z scores)**		DASH[1] diet versus control diet with matching macronutrient contents evidence **(Han 2017)**	Low-moderate GI diet versus moderate-high GI diet **(Han 2017)** Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)** Soy protein-enriched diet versus no soy protein diet **(Han 2017)**
41.0 Length and z score **(None of the included reviews reported data for length z scores)**			Low-moderate GI diet versus moderate-high GI diet **(Han 2017)** DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)**

Secondary Outcomes - Fetal/neonatal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
			Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)**
			Soy protein-enriched diet versus no soy protein diet **(Han 2017)**
			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
			Exercise versus control **(Brown 2017c)**
42.0 Ponderal index		DASH[1] diet versus control diet with matching macronutrient contents **(Han 2017)**	Metformin versus glibenclamide evidence **(Brown 2017a)**
			Low-moderate GI diet versus moderate-high GI diet **(Han 2017)**
			Low-GI diet versus high-fibre moderate-GI diet **(Han 2017)**
			Intensive management versus routine care **(Han 2012)**
43.0 Adiposity (including skinfold thickness measurements (mm), fat mass)			Lifestyle intervention versus usual care or diet alone (whole-body neonatal fat mass) **(Brown 2017b)**
44.1 Neonatal hypoglycaemia (not defined in the reviews)		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Induction of labour versus expectant management **(Boulvain 2001)**
			Glibenclamide versus placebo **(Brown 2017a)**
			4 g myo-inositol + 400 mcg folic acid orally per day and exercise and dietary advice versus placebo 400 mcg folic acid orally per day and exercise and dietary advice **(Brown 2016a)**
			Energy restricted diet versus no energy restricted diet **(Han 2017)**
			Low-carbohydrate diet versus high-carbohydrate diet **(Han 2017)**
			Ethnic specific diet versus standard healthy diet **(Han 2017)**
			Exercise versus control **(Brown 2017c)**
44.2 Neonatal hypoglycaemia (defined)			Metformin versus glibenclamide (BGL < 2.2 mmol/L; < 40 mg/dL) **(Brown 2017a)**
			Glibenclamide versus acarbose (BGL < 2.2 mmol/L; < 40 mg/dL) **(Brown 2017a)**

Secondary Outcomes - Fetal/neonatal	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
			Soy protein-enriched diet versus no soy protein diet (BGL < 1.7 mmol/L (< 30.6 mg/dL) **(Han 2017)**
			Intensive management versus routine care evidence (BGL < 1.7 mmol/L in two consecutive measurements (one trial) and as BGL < 1.94 mmol/L (one trial)) **(Han 2012)**
45.0 Respiratory distress syndrome (RDS)		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Induction of labour versus expectant management **(Boulvain 2001)**
			Metformin versus glibenclamide **(Brown 2017a)**
			Glibenclamide versus acarbose **(Brown 2017a)**
			Ethnic specific diet versus standard healthy diet **(Han 2017)**
			Exercise versus control **(Brown 2017c)**
46.0 Neonatal jaundice (hyperbilirubinaemia) (as defined in the reviews)		Metformin versus glibenclamide **(Brown 2017a)**	Glibenclamide versus placebo **(Brown 2017a)**
		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Energy restricted diet versus no energy restricted diet **(Han 2017)**
			Soy protein-enriched diet versus no soy protein diet **(Han 2017)**
			Ethnic specific diet versus standard healthy diet **(Han 2017)**
			Exercise versus control **(Brown 2017c)**
			Intensive management versus routine care (plasma bilirubin at least 205 µmol/l (one trial) and plasma bilirubin at least 670 µmol/l (one trial)) **(Han 2012)**
47.0 Hypocalcaemia		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Energy restricted diet versus no energy restricted diet **(Han 2017)**
			Ethnic specific diet versus standard healthy diet **(Han 2017)**
			Exercise versus control **(Brown 2017c)**
48.0 Polycythaemia			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**

Secondary Outcomes - Later infant/childhood	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
49.0 Weight and z scores (The included review did not reported data for weight z scores)			Lifestyle intervention versus usual care or diet alone (at 4 to 5 years of age) **(Brown 2017b)**
50.0 Height and z scores (The included review did not reported data for height z scores)			Lifestyle intervention versus usual care or diet alone (at 4 to 5 years of age) **(Brown 2017b)**
51.1 Adiposity: Childhood BMI		Lifestyle intervention versus usual care or diet alone (at 4 to 5 years of age (one trial); 7 to 11 years of age (one trial; 5 to 10 years of age (one trial)) **(Brown 2017b)**	
51.1.2 Adiposity: Childhood BMI z score			Lifestyle intervention versus usual care or diet alone (at 4 to 5 years of age) **(Brown 2017b)**
53.1 Impaired glucose tolerance: fasting blood glucose			Lifestyle intervention versus usual care or diet alone (at 7 to 11 years of age) **(Brown 2017b)**
53.2 Impaired glucose tolerance: two-hour post-prandial blood glucose			Lifestyle intervention versus usual care or diet alone (2 hours post prandial) (7 to 11 years of age) **(Brown 2017b)**
54.1 1 Dyslipidaemia or metabolic syndrome: Total cholesterol			Lifestyle intervention versus usual care or diet alone (at 7 to 11 years of age) **(Brown 2017b)**
54.2 Dyslipidaemia or metabolic syndrome: LDL[1] cholesterol			Lifestyle intervention versus usual care or diet alone (at 7 to 11 years of age) **(Brown 2017b)**
54.3 Dyslipidaemia or metabolic syndrome: HDL[2] cholesterol			Lifestyle intervention versus usual care or diet alone (at 7 to 11 years of age) **(Brown 2017b)**

Secondary Outcomes - Health service use	Benefit	No clear difference	Harm
Overview Review Outcomes	**High Quality Evidence**	**Moderate Quality Evidence**	**Low or Very Low-Quality Evidence**
56.0 Number of antenatal visits or admissions		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	Soy protein-enriched diet versus no soy protein diet **(Han 2017)**
57.1 Visits with dietitian nurse)		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	
57.2 Visits with diabetes educator		Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**	
57.3 Visits with obstetrician			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
57.4 Visits with healthcare provider (not specified)			Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
58.0 Admission to neonatal intensive care unit/nursery			Glibenclamide versus placebo **(Brown 2017a)** Metformin versus glibenclamide **(Brown 2017a)** Soy protein-enriched diet versus no soy protein diet **(Han 2017)**
		Intensive management versus routine care **(Han 2012)**	Lifestyle intervention versus usual care or diet alone **(Brown 2017b)**
59.0 Length of postnatal stay (baby)			Diet recommendation + diet-related behavioural advice versus diet recommendation only **(Han 2017)**

[1]LDL is an acronym for **L**ow **D**ensity **L**ipoprotein cholesterol
[2]HDL is an acronym for **H**igh-**D**ensity **L**ipoprotein cholesterol

Primary outcomes - Maternal

1.0 Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia as defined in reviews)

Hypertensive disorders of pregnancy were reported using various outcomes (any hypertensive disorder, not defined; pregnancy induced hypertension; severe pregnancy-induced hypertension or pre-eclampsia; pre-eclampsia; eclampsia) at the end of pregnancy by five reviews (Brown 2017a; Brown 2017b; Brown 2017c; Han 2012; Han 2017) (Table 2.8; Table 2.18). The quality of the evidence ranged from *moderate- to very low-quality.* There was no clear evidence of a difference between groups reported for any comparison for any hypertensive disorders of pregnancy; not defined; pregnancy-induced hypertension; severe pregnancy-induced hypertension or pre-eclampsia; pre-eclampsia or eclampsia.

1.1 Any hypertensive disorders of pregnancy (not defined)

1.1.1 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of any hypertensive disorder of pregnancy for women with GDM between the glibenclamide and the placebo group (RR 1.24; 95% CI 0.81 to 1.90; one trial, 375 women; *very low-quality evidence*) (Brown 2017a).

1.1.2 Metformin versus glibenclamide: There was no clear difference for the risk of any hypertensive disorder of pregnancy for women with GDM between metformin and glibenclamide group (RR 0.70; 95% CI 0.38 to 1.30; three trials, 508 women; *moderate-quality* evidence) (Brown 2017a).

Summary

Probably no difference between interventions: direction of effect suggest benefit, but more evidence is needed

- *Moderate-quality* evidence showed no clear difference for women with GDM for the treatment with metformin versus glibenclamide for the risk of any hypertensive disorders of pregnancy.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence showed no clear difference for the treatment with glibenclamide versus placebo for women with GDM for the risk of any hypertensive disorder of pregnancy.

1.2 Pregnancy induced hypertension

1.2.1 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of pregnancy induced hypertension for women with GDM between the glibenclamide and the placebo group (RR 1.24,

95% CI 0.71 to 2.19; one trial, 375 women; *low-quality evidence*) (Brown 2017a). Pregnancy induced hypertension was defined as persistent systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg.

1.2.2 Metformin versus glibenclamide: There was no clear difference for the risk of pregnancy induced hypertension (not defined) for women with GDM between the metformin and glibenclamide group (RR 0.71, 95 % CI 0.37 to 1.37; two trials, 359 women; *moderate-quality evidence*) (Brown 2017a).

1.2.3 Low carbohydrate diet versus high carbohydrate diet: There was no clear difference for the risk of maternal hypertension in pregnancy (not defined) for women with GDM between the low carbohydrate diet and high carbohydrate diet group (RR 0.40, 95 % CI 0.13 to 1.22; one trial, 150 women; *very low-quality evidence*) (Han 2017).

1.2.4 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for the risk of maternal hypertension in pregnancy (not defined) for women with GDM between the high unsaturated fat diet versus low unsaturated fat diet with matching calories group (RR 0.54, 95 % CI 0.06 to 5.26; one trial, 27 women; *very low-quality evidence*) (Han 2017).

1.2.5 Ethnic specific diet versus standard healthy diet: There was no clear difference for the risk of maternal hypertension in pregnancy (not defined) for women with GDM between the ethnic specific diet and standard healthy diet group (RR 0.33, 95 % CI 0.02 to 7.32; one trial, 20 women; *very low-quality evidence*) (Han 2017).

Summary

Probably no difference between interventions: direction of effect suggest benefit, but more evidence is needed

- *Moderate-quality* evidence showed no clear difference for women with GDM for the treatment with metformin versus glibenclamide for the risk of pregnancy induced hypertension.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the treatment with glibenclamide versus placebo for women with GDM for the risk of pregnancy induced hypertension.
- *Very low-quality* evidence showed no clear difference for the treatment with low carbohydrate diet versus high carbohydrate diet; high unsaturated fat diet versus low unsaturated fat diet with matching calories; and ethnic specific diet versus standard healthy diet for women with GDM for the risk of pregnancy induced hypertension.

1.3 Severe pregnancy-induced hypertension or pre-eclampsia

1.3.1 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of severe pregnancy induced hypertension or pre-eclampsia for women with GDM between glibenclamide and the placebo group (1.23, 95% CI 0.59 to 2.56; one trial, 375 women; *low-quality evidence*) (Brown 2017a). Severe pregnancy induced hypertension or pre-eclampsia was defined as proteinuria ≥ 2 g in 24 hours, or ≥ 2+ on dipstick, blood pressure ≥ 160 mmHg or diastolic pressure ≥ 110 mmHg, serum creatinine > 1.0 mg/dL, platelets < 100,000 mm^3, asparate aminotransferase > 90 units/L, or symptoms such as persistent headache, scotomata or epigastric pain.

1.3.2 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the risk of severe hypertension (not defined) or pre-eclampsia for women with GDM between the low-moderate GI diet and the moderate-high GI diet group (RR 1.02; 95% CI 0.07 to 15.86; one trial, 95 women; *very low-quality evidence*) (Han 2017).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the treatment with glibenclamide versus placebo for women with GDM for the risk of severe hypertension or pre-eclampsia combined.
- *Very low-quality* evidence showed no clear difference for the treatment with low-moderate GI diet versus moderate-high GI diet for women with GDM for the risk of severe hypertension or pre-eclampsia combined.

1.4 Pre-eclampsia (not defined)

1.4.1 Metformin versus Glibenclamide: There was no clear difference for the risk of pre-eclampsia for women with GDM between metformin and glibenclamide group (RR 0.66, 95 % CI 0.11 to 3.82; one trial, 149 women; *very low-quality evidence*) (Brown 2017a).

1.4.2 Energy restricted diet versus no energy restricted diet: There was no clear difference for the risk of pre-eclampsia for women with GDM between the energy restricted diet and no energy restricted diet group (RR 1.00; 95% CI 0.51 to 1.97; one trial, 117 women; *low quality evidence*) (Han 2017).

1.4.3 DASH diet versus control diet with matching macronutrient contents: There was no clear difference for the risk of pre-eclampsia for women with GDM between the DASH and the control diet with matching macronutrient contents group (RR 1.00, 95% CI 0.31 to 3.26; three trials, 136 women;

moderate-quality evidence) (Han 2017). (**DASH** is an acronym for **D**ietary **A**pproaches to **S**top **H**ypertension).

1.4.4 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no events of pre-eclampsia for women with GDM in either the high unsaturated fat or the low unsaturated fat diet with matching calories group (RR not estimable; one trial, 27 women; *low-quality evidence*) (Han 2017).

1.4.5 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for the risk of pre-eclampsia for women with GDM between the soy protein-enriched and the no soy protein diet group (RR 2.00, 95 % CI 0.19 to 21.03; one trial, 68 women; *very low-quality evidence*) (Han 2017).

1.4.6 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of pre-eclampsia for women with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.70, 95% CI 0.40 to 1.22; four trials, 2796 women; *low-quality evidence*) (Brown 2017b).

1.4.7 Exercise versus control: There was no clear difference for the risk of pre-eclampsia for women with GDM between the exercise and control group (RR 0.31, 95% CI 0.01 to 7.09; two trials, 48 women; *low-quality evidence*) (Brown 2017c).

1.4.8 Intensive management versus routine care: There was no clear difference for the risk of pre-eclampsia for women with GDM between the intensive management and routine care group (RR 2.74; 95% CI 0.26 to 29.07; one trial, 83 women; *low-quality evidence*) (Han 2012).

Summary

Probably ineffective interventions (more evidence needed): indicating that the review found moderate-quality evidence suggesting lack of effectiveness for an intervention, more evidence needed

- *Moderate-quality* evidence showed no clear difference for women with GDM for the treatment with the DASH diet versus control diet with matching macronutrient contents for the risk of pre-eclampsia. Insufficient evidence available.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the treatment with energy restricted diet versus no energy restricted diet; high unsaturated fat diet versus low unsaturated fat diet with matching calories; lifestyle intervention versus usual care or diet alone; exercise versus control; and intensive management versus routine care for women with GDM for the risk of pre-eclampsia.

Summary

- *Very low-quality* evidence showed no clear difference for the treatment with metformin versus glibenclamide; or soy protein-enriched diet versus no soy protein diet for women with GDM for the risk of pre-eclampsia.

1.5 Eclampsia (not defined)

1.5.1 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the risk of eclampsia for women with GDM between a low-moderate GI diet and moderate-high GI diet group (RR 0.34; 95% CI 0.01 to 8.14, one trial 83 women; *very low-quality evidence*) (Han 2017).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence showed no clear difference for the risk of eclampsia with the treatment with low-moderate GI diet versus moderate-high GI diet.

2.0 Caesarean section

Caesarean section was reported as an outcome in seven reviews (Boulvain 2001; Brown 2017a; Brown 2017b; Brown 2017c; Han 2012; Han 2017; Martis 2016a) (Table 2.8; Table 2.18). The quality of the evidence ranged from *moderate- to very low-quality.*

2.1 Induction of labour versus expectant management: There was no clear difference for the risk of birth by caesarean section for women with GDM between induction of labour and expectant management group (RR 0.81, 95% CI 0.52 to 1.26; one trial, 200 women; *low-quality evidence*) (Boulvain 2001).

2.2 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of birth by caesarean section for women with GDM between the glibenclamide and placebo group (RR 1.03, 95% CI 0.79 to 1.34; one trial, 375 women; *very low-quality evidence*) (Brown 2017a).

2.3 Metformin versus glibenclamide: There was no clear difference for the risk of birth by caesarean section for women with GDM between the metformin and glibenclamide group (average RR 1.20, 95% CI 0.83 to 1.72; four trials, 554 women; *low-quality evidence*) (Brown 2017a).

2.4 Glibenclamide versus acarbose: There was no clear difference for the risk of birth by caesarean section for women with GDM between the glibenclamide and acarbose group (RR 0.95, 95% CI 0.53 to 1.70; one trial, 43 women; *low-quality evidence*) (Brown 2017a).

2.5 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the risk of birth by caesarean section for women with GDM between the low-moderate GI diet and moderate-high GI diet group (RR 0.66, 95% CI 0.29 to 1.47; one trial, 63 women; *very low-quality evidence*) (Han 2017).

2.6 Energy restricted diet versus no energy restricted diet: There was no clear difference for the risk of birth by caesarean section for women with GDM between the energy restricted diet and no energy restricted diet group (RR 1.12, 95% CI 0.80 to 1.56; two trials, 420 women; *low-quality evidence*) (Han 2017).

2.7 DASH diet versus control diet with matching macronutrient contents: There was evidence for a reduction for the risk of birth by caesarean section for women with GDM in the DASH diet group compared to the control diet with matching macronutrient contents group (RR 0.53, 95% CI 0.37 to 0.76; two trials, 86 women; *moderate-quality evidence*) (Han 2017).

2.8 Low carbohydrate diet versus high-carbohydrate diet: There was no clear difference for the risk of birth by caesarean section for women with GDM between the low carbohydrate diet and high-carbohydrate diet group (RR 1.29, 95% CI 0.84 to 1.99; two trials, 179 women; *low-quality evidence*) (Han 2017).

2.9 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for the risk of birth by caesarean section for women with GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (RR 1.08, 95% CI 0.07 to 15.50; one trial, 27 women; *very low-quality evidence*) (Han 2017).

2.10 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for the risk of birth by caesarean section for women with GDM between the low-GI diet and high-fibre moderate-GI diet group (RR 1.91, 95% CI 0.91 to 4.03; one trial, 92 women; *low-quality evidence*) (Han 2017).

2.11 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference for the risk of birth by caesarean section for women with GDM between

the diet recommendation + diet-related behavioural advice and diet recommendation only group (RR 0.78, 95% CI 0.38 to 1.62; one trial, 99 women; *low-quality evidence*) (Han 2017).

2.12 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for the risk of birth by caesarean section for women with GDM between the soy protein-enriched diet and no soy protein diet group (RR 1.00, 95% CI 0.57 to 1.77; one trial 68 women; *low-quality evidence*) (Han 2017).

2.13 Ethnic specific diet versus standard healthy diet: There was no clear difference for the risk of birth by caesarean section for women with GDM between the ethnic specific diet and standard healthy diet group (RR 1.20, 95% CI 0.54 to 2.67; one trial, 20 women; *very low-quality evidence*) (Han 2017).

2.14 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of birth by caesarean section for women with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.90, 95% CI 0.78 to 1.05; 10 trials, 3545 women; *low-quality evidence*) (Brown 2017b).

2.15 Exercise versus control: There was no clear difference for the risk of birth by caesarean section for women with GDM between the exercise and control group (RR 0.86, 95% CI 0.63 to 1.16; five trials, 316 women; *moderate-quality evidence*) (Brown 2017c).

2.16 Intensive management versus routine care: There was no clear difference for the risk of birth by caesarean section for women with GDM between the intensive management and routine care group (RR 0.93, 95% CI 0.68 to 1.27; three trials, 509 women; *very low-quality evidence*) (Han 2012).

2.17 Strict intensity of glycaemic control versus less strict glycaemic control: There was no clear difference for the risk of birth by caesarean section for women with GDM between the strict intensity of glycaemic control and less strict glycaemic control group (RR 1.35, 95% CI 0.83 to 2.18; one trial, 171 women; *very low-quality evidence*) (Martis 2016a).

Summary

Promising interventions: moderate quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence of benefit suggested a benefit by a reduction for the risk of birth by caesarean section for women with GDM who were treated with the DASH diet compared to the control diet with matching macronutrient contents group.

Summary

- *Moderate-quality* evidence showed no clear difference (the direction of the effect suggested benefit) for the treatment with exercise versus control for women with GDM for the risk of birth by caesarean section.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the treatment with induction of labour versus expectant management; metformin versus glibenclamide; glibenclamide versus acarbose; energy restricted diet versus no energy restricted diet; low carbohydrate diet versus high-carbohydrate diet; low-GI diet versus high-fibre moderate-GI diet; diet recommendation + diet-related behavioural advice versus diet recommendation only; soy protein-enriched diet versus no soy protein diet; and lifestyle intervention versus usual care or diet alone for women with GDM for the risk of birth by caesarean section.
- *Very low-quality* evidence showed no clear difference for the treatment with glibenclamide versus placebo; low-moderate GI diet versus moderate-high GI diet; high unsaturated fat diet versus low unsaturated fat diet with matching calories; ethnic specific diet versus standard healthy diet; intensive management versus routine care; and strict intensity of glycaemic control versus less strict glycaemic control for women with GDM for the risk of birth by caesarean section.

3.0 Development of type 2 diabetes

Development of type 2 diabetes was reported as an outcome by two reviews (Brown 2017b; Han 2017) (Table 2.8; Table 2.18). Time points for testing for type two diabetes ranged from one to two weeks postpartum (Han 2017) up to 13 months post-partum (Han 2017). The Brown 2017b review did not define the test or the time point. The quality of the evidence ranged from *low- to very low-quality.* There was no clear evidence of a difference for the risk of development of type 2 diabetes for any of the comparisons reporting this outcome.

3.1 OGTT (Oral Glucose Tolerance Test) for diagnosis of type 2 diabetes

3.1.1 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for the risk of developing type 2 diabetes at one to two weeks postpartum, (RR 2.00, 95% CI 0.45 to 8.94; one trial, 24 women; *very low-quality evidence*) or at four to 13 months postpartum (RR 1.00, 95% CI 0.10 to 9.61; one trial, 6 women; v*ery low-quality* evidence) for women with GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (Han 2017).

3.1.2 Low-GI diet versus high fibre moderate-GI diet: There was no clear difference for the risk of developing type 2 diabetes at three months postpartum, for women with GDM between the low-GI diet

versus high fibre moderate-GI diet group (RR 0.76, 95% CI 0.11 to 5.01; one trial, 58 women; *very low-quality evidence*) (Han 2017).

3.1.3 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of developing type 2 diabetes (test and time frame not defined in the review) for women with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.98, 95% CI 0.54 to 1.76; two trials, 486 women; *low-quality evidence*) (Brown 2017b).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the treatment with lifestyle intervention versus usual care or diet alone for women with GDM for the risk of developing type 2 diabetes (diagnostic test or timeframe not defined).
- *Very low-quality* evidence showed no clear difference for the treatment with high unsaturated fat diet versus low unsaturated fat diet with matching calories for women with GDM or the risk of developing type 2 diabetes using the OGTT (Oral Glucose Tolerance Test) for diagnosis of type 2 diabetes at one- to two-weeks post-partum or at four to 13 months post-partum. There was no clear difference for the treatment with low-GI diet versus high fibre moderate-GI diet for women with GDM for the risk of developing type 2 diabetes using the OGTT at three months post-partum.

Primary outcomes - Neonatal

4.0 Perinatal (fetal and neonatal death) and later infant mortality

Perinatal (fetal and neonatal death) and later infant mortality was an outcome that was reported by five reviews (Boulvain 2001; Brown 2017a; Brown 2017b; Brown 2017c; Han 2017) (Table 2.9; Table 2.18). All five reviews reported perinatal mortality. None reported on later infant mortality. The quality of the evidence ranged from *low- to very low-quality.* There was no clear evidence of a difference for the risk of perinatal mortality for any of the comparisons reporting this outcome.

4.1 Induction of labour versus expectant management: There were no events of perinatal mortality recorded for babies born to mothers with GDM in either the induction of labour or the expectant management group (RR not estimable; one trial, 200 babies; *very low-quality evidence*) (Boulvain 2001).

4.2 Metformin versus glibenclamide: There was no clear difference for the risk of perinatal mortality for babies born to mothers with GDM between the metformin and glibenclamide group (average RR

0.92, 95% CI 0.06 to 14.55; two trials, 359 babies; *very low-quality evidence*) (Brown 2017a). There were no deaths in each group in one trial and one death in each group for the second trial.

4.3 Glibenclamide versus acarbose: There were no perinatal deaths for babies whose mothers were treated with either glibenclamide or acarbose (RR not estimable; one trial, 43 babies; *low-quality evidence*) (Brown 2017a).

4.4 Energy restricted diet versus no energy restricted diet: There were no perinatal deaths reported for babies born to mothers with GDM who were treated with the energy restricted diet or the no energy restricted diet group (RR not estimable; two trials, 423 babies; *low-quality evidence*) (Han 2017).

4.5 Low carbohydrate diet versus high-carbohydrate diet: There was no clear difference for the risk of perinatal mortality for babies born to mothers with GDM between the low carbohydrate diet and high-carbohydrate diet group (RR 3.00, 95% CI 0.12 to 72.49; one trial, 150 babies; *very low-quality evidence*) (Han 2017). There was one event in the control group.

4.6 Lifestyle intervention versus usual care or diet alone: There was no clear difference and substantial uncertainty about the size and the direction of effect for perinatal mortality for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.09, 95% CI 0.01 to 1.70; two trials, 1988 babies; *low-quality evidence*) (Brown 2017b). One trial had no events and one trial had 5 events in the control group.

4.7 Exercise versus control: There were no events of perinatal deaths reported for babies born to mothers with GDM who were treated either in the exercise or the control group (RR not estimable; one trial, 19 babies; *low-quality evidence*) (Brown 2017c).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the risk of perinatal mortality for babies born to mothers with GDM who were treated with glibenclamide versus acarbose; energy restricted diet versus no energy restricted diet; lifestyle intervention versus usual care; or diet alone or exercise versus control.
- *Very low-quality* evidence showed no clear difference for the risk of perinatal mortality for babies born to mothers with GDM who were treated with induction of labour versus expectant

management; metformin versus glibenclamide; or low carbohydrate diet versus high-carbohydrate diet for women with GDM for the risk of perinatal mortality.

5.0 Large-for-gestational age (LGA) (defined as > 90th percentile in all included reviews)

Large-for-gestational age (LGA) was reported as an outcome by six reviews (Boulvain 2001; Brown 2016a; Brown 2017a; Brown 2017b; Han 2012; Han 2017) (Table 2.9; Table 2.18). The quality of the evidence ranged from *low- to very low-quality.*

5.1 Induction of labour versus expectant management: The evidence suggested a reduction in the risk of LGA for babies whose mothers were induced at 38 completed weeks of gestation compared to the expectant management group (RR 0.43, 95% CI 0.22 to 0.87; one trial, 200 babies; *low-quality evidence*) (Boulvain 2001).

5.2 Oral antidiabetic agents versus placebo: There was no clear difference in the risk of LGA for babies born to mothers with GDM between the glibenclamide and placebo group (RR 0.89, 95% CI 0.51 to 1.58; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

5.3 Metformin versus glibenclamide: There was no clear difference in the risk of LGA for babies born to mothers with GDM between the metformin and glibenclamide group (RR 0.67, 95% CI 0.24 to 1.83; two trials, 246 babies; *low-quality evidence*) (Brown 2017a).

5.4 Glibenclamide versus acarbose: There was no clear difference in the risk of LGA for babies born to mothers with GDM between the glibenclamide and acarbose group (RR 2.38, 95% CI 0.54 to 10.46; one trial, 43 babies; *low-quality evidence*) (Brown 2017a).

5.5 Myo-inositol versus placebo: There was no clear difference in the risk of LGA for babies born to mothers with GDM between the myo-inositol and the placebo group (RR 0.36, 95 % CI 0.02 to 8.58; one trial, 73 babies; *low-quality evidence*) (Brown 2016a).

5.6 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the risk of LGA for babies born to mothers with GDM between the low-moderate GI diet and moderate-high GI diet group (RR 0.71, 95% CI 0.22 to 2.34; two trials, 89 babies; *low-quality evidence*) (Han 2017).

5.7 Energy restricted diet versus no energy restricted diet: There was no clear difference for the risk of LGA for babies born to mothers with GDM between the energy restricted diet and no energy restricted diet group (RR 1.17, 95% CI 0.65 to 2.12; one trial, 123 babies; *low-quality evidence)* (Han 2017).

5.8 Low carbohydrate diet versus high-carbohydrate diet: There was no clear difference for the risk of LGA for babies born to mothers with GDM between the low carbohydrate diet and high-carbohydrate diet group (RR 0.51, 95% CI 0.13 to 1.95; one trial, 149 babies; *very low-quality evidence)* (Han 2017).

5.9 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for the risk of LGA for babies born to mothers with GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (RR 0.54, 95% CI 0.21 to 1.37; one trial, 27 women; *very low-quality* evidence) (Han 2017).

5.10 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for the risk of LGA for babies born to mothers with GDM between the low-GI diet and high-fibre moderate-GI diet group (RR 2.87, 95% CI 0.61 to 13.50; one trial, 92 babies; *very low-quality evidence*) (Han 2017).

5.11 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference for the risk of LGA for babies born to mothers with GDM between the diet recommendation + diet-related behavioural advice and diet recommendation only group (RR 0.73, 95% CI 0.25 to 2.14; one trial, 99 babies; *very low-quality evidence*) (Han 2017).

5.12 Ethnic specific diet versus standard healthy diet: There was no clear difference for the risk of LGA for babies born to mothers with GDM between the ethnic specific diet and standard healthy diet group (RR 0.14, 95% CI 0.01 to 2.45; one trial, 20 women; *very low-quality evidence*) (Han 2017).

5.13 Lifestyle intervention versus usual care or diet alone: The evidence suggested a reduction in the risk of LGA for babies born to mothers with GDM in the lifestyle intervention compared to the usual care or diet alone group (RR 0.60, 95% CI 0.50 to 0.71; six trials, 2994 babies; *moderate-quality evidence*) (Brown 2017b).

5.14 Intensive management versus routine care: The evidence suggested a reduction in the risk of LGA for babies born to mothers with GDM in the intensive management group compared to the routine care group (RR 0.37, 95% CI 0.20 to 0.66; three trials, 438 babies; *low-quality evidence*) (Han 2012).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence suggested a benefit by a reduction in the risk of LGA for babies born to mothers who were treated with lifestyle intervention compared to the usual care or diet alone.

No conclusions possible: low to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit by a reduction in the risk of LGA for babies born to mothers who were treated with induction of labour compared to expectant management at 38 weeks' complete gestation; or with intensive management compared to routine care. There was no clear evidence of a difference for the risk of being born LGA for babies born to mothers with GDM who were treated with metformin versus glibenclamide; glibenclamide versus acarbose; myo-inositol versus placebo; low-moderate GI diet versus moderate-high GI diet or energy restricted diet versus no energy restricted diet.
- *Very low-quality* evidence showed no clear difference in the risk of LGA for babies born to mothers with GDM who were treated with glibenclamide versus placebo; low carbohydrate diet versus high-carbohydrate diet; high unsaturated fat diet versus low unsaturated fat diet with matching calories; low-GI diet versus high-fibre moderate-GI diet; Diet recommendation + diet-related behavioural advice versus diet recommendation only; or ethnic specific diet versus standard healthy diet for the risk of LGA for the babies.

6.0 Death or serious morbidity composite (as defined in reviews, e.g. perinatal or infant death, shoulder dystocia, bone fracture or nerve palsy)

Death or serious morbidity composite (as defined in reviews, e.g. perinatal or infant death, shoulder dystocia, bone fracture or nerve palsy) was reported as an outcome in four reviews (Brown 2017a; Han 2017; Brown 2017b; Brown 2017c) (Table 2.9; Table 2.18). The components of the composite differed between trials. The quality of the evidence ranged from moderate- *to very low-quality.*

6.1 Metformin versus glibenclamide: The evidence suggested a reduction in the risk of a death or serious morbidity composite outcome for babies born to mothers with GDM in the metformin group compared to the glibenclamide group (RR 0.54, 95% CI 0.31 to 0.94; one trial, 159 babies; *low-quality evidence*) (Brown 2017a). The morbidity composite included hypoglycaemia, hyperbilirubinaemia, macrosomia, respiratory illness, birth injury, stillbirth or neonatal death.

6.2 Ethnic specific diet versus standard healthy diet: There were no babies in either group that experienced morbidity composite outcomes whose mothers were treated with the ethnic specific diet or the standard healthy diet group (RR not estimable; one trial, 20 babies; *very low-quality evidence*) (Han 2017). The morbidity composite included hypoglycaemia, neonatal asphyxia, respiratory distress syndrome, hyperbilirubinaemia and hypocalcaemia.

6.3 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of a death or serious morbidity composite outcome for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (average RR 0.57, 95% CI 0.21 to 1.55; two trials, 1930 babies; *very low-quality evidence*) (Brown 2017b). The death or serious morbidity composite included death, shoulder dystocia, bone fracture and nerve palsy in one trial and in the other trial included stillbirth, neonatal death, hypoglycaemia, hyperbilirubinaemia, elevated cord-blood C-peptide and birth trauma. The authors of the review decided to include both trials in the meta-analysis as the direction of the treatment effect is the same for both trials.

6.4 Exercise versus control: There was no clear difference for the risk of a death or serious morbidity composite outcome for babies born to mothers with GDM between the exercise and control group (RR 0.56, 95% CI 0.12 to 2.61; two trials, 169 babies; *moderate-quality evidence)* (Brown 2017c).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed no clear difference in the risk of death or serious morbidity composite outcomes for babies born to mothers with GDM who were treated with exercise versus control.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit by a reduction in the risk of death or serious morbidity composite outcomes for babies born to mothers with GDM who were treated with metformin compared to glibenclamide.
- *Very low-quality* evidence showed no clear difference in the risk of death or serious morbidity composite outcomes for babies born to mothers with GDM who were treated with ethnic specific diet versus standard healthy diet or with lifestyle intervention versus usual care or diet alone.

7.0 Neurosensory disability in later childhood (as defined in reviews)

None of the included reviews reported data for neurosensory disability in later childhood as either a primary or a secondary outcome.

Secondary outcomes - Maternal

8.0 Use of additional pharmacotherapy

The use of additional pharmacotherapy was reported as an outcome by seven reviews (Brown 2016a; Brown 2017a; Han 2017; Brown 2017b; Brown 2017c; Han 2012; Martis 2016a) (Table 2.11; Table 2.19). The quality of the evidence ranged from *high- to very low-quality.*

8.1 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of requiring additional pharmacotherapy (insulin) for women with GDM between the oral antidiabetic agent (glibenclamide or acarbose) and placebo group (RR 0.68, 95% CI 0.42 to 1.11; two trials, 434 women; *low-quality evidence*) (Brown 2017a). A further included trial in the review reported that "15/19 women in the standard care group were prescribed metformin and two women required insulin. However, it is not clear if any women in the metformin group required supplementary insulin".

8.2 Metformin versus glibenclamide: There was no difference for the risk of requiring additional pharmacotherapy (insulin) for women with GDM between the metformin and glibenclamide group (RR 0.66; 95% CI 0.28 to 1.57; five trials, 660 women; *very low-quality evidence*) (Brown 2017a).

8.3 Glibenclamide versus acarbose: There was no clear difference for the risk of requiring additional pharmacotherapy (insulin) for women with GDM between the glibenclamide and acarbose group (RR 0.49, 95% CI 0.19 to 1.27; one trial, 43 women; *low-quality evidence*) (Brown 2017a).

8.4 Myo-inositol versus placebo: There was no clear difference for the risk of requiring additional pharmacotherapy (insulin) for women with GDM between the myo-inositol and the placebo group (average RR 0.37, 95 % CI 0.08 to 1.73; two trials, 157 women; *low-quality evidence*) (Brown 2016a).

8.5 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the use of additional pharmacotherapy (not defined) for women with GDM between the low-moderate GI diet and moderate-high GI diet group (RR 0.82, 95% CI 0.39 to 1.74; four trials, 221 women; *low-quality evidence*) (Han 2017).

8.6 Energy restricted diet versus no energy restricted diet: Meta-analysis was not possible for this outcome due to substantial heterogeneity (I^2 = 94%). One trial was judged to be of *very low-quality* evidence (Han 2017) and showed no clear difference for the use of additional pharmacotherapy (insulin)

for women with GDM between the energy restricted diet and no energy restricted diet group (RR 1.05, 95% CI 0.47 to 2.34; one trial, 117 women).

The use of insulin in the second trial was only part of the protocol for the energy-restricted diet intervention group, and thus accordingly there were more cases of additional pharmacotherapy use in this group (36/149 versus 0/150 in the energy-restricted diet and no energy-restricted diet groups, respectively) (RR 73.49, 95% CI 4.55 to 1186.39; one trial, 299 women; *very low-quality*).

8.7 DASH diet versus control diet with matching macronutrient contents: The evidence suggested a reduced use of additional pharmacotherapy (not defined) for women with GDM in the DASH diet group compared to the control diet with matching macronutrient contents group (RR 0.28, 95% CI 0.14 to 0.53; two trials, 86 women; *moderate-quality evidence*) (Han 2017).

8.8 Low carbohydrate diet versus high-carbohydrate diet: There was no clear difference for the use of additional pharmacotherapy (not defined) for women with GDM between the low carbohydrate diet and high-carbohydrate diet group (RR 1.02, 95% CI 0.77 to 1.37; two trials, 180 women; *low-quality evidence*) (Han 2017).

8.9 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There were no events of the use of additional pharmacotherapy (not defined) for women with GDM in either the high unsaturated fat diet or the low unsaturated fat diet with matching calories group (RR not estimable; two trials, 111 women; *low-quality evidence*) (Han 2017).

8.10 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for the use of additional pharmacotherapy (not defined) for women with GDM between the low-GI diet and high-fibre moderate-GI diet group (RR 0.83, 95% CI 0.58 to 1.17; one trial, 92 women; *low-quality evidence*) (Han 2017).

8.11 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference for the use of additional pharmacotherapy (not defined) for women with GDM between the diet recommendation + diet-related behavioural advice and diet recommendation only group (RR 0.61, 95% CI 0.15 to 2.42; one trial, 99 women; *very low-quality evidence*) (Han 2017).

8.12 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for the use of additional pharmacotherapy (not defined) for women with GDM between the soy protein-enriched diet

and the no soy protein diet group (RR 1.00, 95 % CI 0.15 to 6.70; one trial, 68 women; *very low-quality evidence*) (Han 2017).

8.13 High-fibre diet versus standard-fibre diet: There were no events of the use of additional pharmacotherapy (not defined) for women with GDM in either the high-fibre diet or the standard-fibre diet (RR not estimable; one trial, 22 women; *low-quality evidence*) (Han 2017).

8.14 Ethnic specific diet versus standard healthy diet: There was no clear difference for the use of additional pharmacotherapy (not defined) for women with GDM between the ethnic specific diet and standard healthy diet group (RR 2.00, 95% CI 0.21 to 18.69; one trial, 20 women; *very low-quality evidence*) (Han 2017).

8.15 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the use of additional pharmacotherapy (oral antidiabetic agents) for women with GDM between the lifestyle intervention and usual care or diet alone group (average RR 0.79, 95% CI 0.52 to 1.19; one trial, 197 women; m*oderate-quality evidence*) (Brown 2017b).

8.16 Lifestyle intervention versus usual care or diet alone: The evidence suggested an increased risk of needing additional pharmacotherapy (insulin) for women with GDM in the lifestyle intervention group compared to the usual care or diet alone group (average RR 2.54, 95% CI 1.19 to 5.42; nine trials, 3254 women; *very low-quality evidence*) (Brown 2017b).

8.17 Exercise versus control: There was no clear difference in the risk of needing additional pharmacotherapy (one trial defined as insulin, others not defined) for women with GDM between the exercise and control group (RR 0.76, 95% CI 0.54 to 1.08; seven trials, 413 women; *moderate-quality evidence*) (Brown 2017c).

8.18 Intensive management versus routine care: There was no clear difference in the risk of needing additional pharmacotherapy (defined as insulin or oral hypoglycaemic agents in the review) for women with GDM between the intensive management and routine care group (RR 1.00, 95% CI 0.30 to 3.32; one trial, 12 women; *very low-quality evidence*) (Han 2012).

8.19 Strict intensity of glycaemic control versus less strict glycaemic control: The evidence suggested an increased risk of needing additional pharmacotherapy (insulin) for women with GDM in

the strict intensity of glycaemic control group compared to the less strict glycaemic control group (RR 1.85, 95% CI 1.14 to 3.03; one trial, 171 women; *very low-quality evidence*) (Martis 2016a).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed no clear difference for the use of additional pharmacotherapy for women with GDM who were treated with lifestyle interventions versus usual care or diet alone (the additional pharmacotherapy being the oral antidiabetic agents glibenclamide and acarbose); the DASH diet compared to the control diet with matching macronutrient contents (additional pharmacotherapy not defined in the review) or exercise versus control (the additional pharmacotherapy being insulin one trial, others not defined).

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the use of additional pharmacotherapy for women who were treated with glibenclamide versus placebo; acarbose versus placebo; glibenclamide versus acarbose; myo-inositol versus placebo; low-moderate GI diet versus moderate-high GI diet; low carbohydrate diet versus high-carbohydrate diet or low-GI diet versus high-fibre moderate-GI diet. There were no events reported in either group for high unsaturated fat diet versus low unsaturated fat diet with matching calories or high-fibre diet versus standard-fibre diet.
- *Very low-quality* evidence suggested an increase in the use of insulin for women who were treated with lifestyle interventions compared to usual care or diet alone; or strict intensity of glycaemic control compared to less strict glycaemic control.
- *Very low-quality* evidence showed no clear difference for the use of additional pharmacotherapy for women who were treated with metformin versus glibenclamide; or energy restricted diet versus no energy restricted diet; diet recommendation + diet-related behavioural advice versus diet recommendation only; soy protein-enriched diet versus no soy protein diet; or ethnic specific diet versus standard healthy diet or intensive management versus routine care.

9.0 Maternal hypoglycaemia (as defined in the reviews)

Maternal hypoglycaemia was reported as an outcome by four reviews (Brown 2017a; Brown 2017b; Brown 2017c; Han 2017). Maternal hypoglycaemia was only defined in one of three trials within the Brown 2017a review. None of the remaining reviews included definitions of maternal hypoglycaemia (Table 2.11; Table 2.19). The quality of the evidence ranged from *low- to very low-quality.* There was no clear evidence of a difference for the risk of maternal hypoglycaemia for any of the comparisons reporting this outcome.

9.1 Metformin versus glibenclamide: There was no clear difference for the risk of maternal hypoglycaemia for women with GDM between the metformin and glibenclamide group (RR 0.89; 95% CI 0.36 to 2.19; three trials, 354 women; *low-quality evidence*) (Brown 2017a). One of the three trials

defined maternal hypoglycaemia as < 3.3 mmol/L (60 mg/dL). One further trial was excluded from this analysis, "currently published as a conference abstract, reported data for women who dropped out of the study with hypoglycaemia. 39% of women in the glibenclamide group (17/45) and 3% of women in the metformin group (1/36) “dropped out” of the study due to maternal hypoglycaemia. It is unclear whether they withdrew from the study due to treatment side effects or were lost to follow-up".

9.2 Glibenclamide versus acarbose: There were no events for maternal hypoglycaemia in either the glibenclamide or acarbose treated group (RR not estimable; one trial, 43 women; *low-quality evidence*) (Brown 2017a).

9.3 High-fibre diet versus standard-fibre diet: There was no clear difference for the risk of maternal hypoglycaemia for women with GDM between the high-fibre diet and standard-fibre diet (recorded as mean numbers of events) (MD -1.00; -2.08 to 0.08; one trial, 22 women; *very low-quality evidence*) (Han 2017).

9.4 Lifestyle intervention versus usual care or diet alone: There were no events for maternal hypoglycaemia in either the lifestyle intervention or usual care or diet group (RR not estimable; one trial, 19 women; *very low-quality evidence*) (Brown 2017b).

9.5 Exercise versus control: There were no events for maternal hypoglycaemia in either the exercise or the control group (RR not estimable; one trial, 34 women; *low-quality* evidence) (Brown 2017c).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the risk of maternal hypoglycaemia for women with GDM who were treated with Metformin versus glibenclamide (defined as < 3.3 mmol/L (60 mg/dL)); or glibenclamide versus acarbose (not defined); or exercise versus control.
- *Very low-quality* evidence showed no clear difference for the risk of maternal hypoglycaemia for women with GDM who were treated with high-fibre diet versus standard-fibre diet (not defined); or lifestyle intervention versus usual care or diet alone (not defined).

10.0 Glycaemic control during/ end of treatment (as defined in the reviews)

Glycaemic control during/end of treatment was reported as an outcome by five reviews (Brown 2016a; Brown 2017a; Brown 2017b; Brown 2017c; Han 2017) (Table 2.11; Table 2.19). The outcome was reported at different time points during or at the end of treatment using the following measures:

Glycaemic control (timing not defined); Glycaemic control during the treatment: pre-prandial/fasting, post-prandial; HbA1c, 24 hour mean plasma glucose; Glycaemic control at the end of treatment: Fasting, one-hour post-prandial, two-hours postprandial, post-prandial timing not defined, mean plasma glucose, HbA1c; Glycaemic control during/at the end of treatment: Fasting, mean plasma glucose, HbA1c.

The time of day for the recording of one-hour and two-hour post-prandial blood glucose measurements also varied with some being recorded after breakfast, and others after lunch or dinner.

The quality of the evidence ranged from *moderate- to very low-quality.*

10.1 Glycaemic control: timing not defined

10.1.1 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference in blood glucose concentration (timing and testing not defined in the review) for women with GDM between the low-GI diet and high-fibre moderate-GI diet group (MD -0.10 mmol/L, 95% CI -0.38 to 0.18; one trial, 74 women; *very low-quality evidence*) (Han 2017).

10.2 Glycaemic control during the treatment: pre-prandial/fasting

10.2.1 Energy restricted diet versus no energy restricted diet: There was no clear difference in pre-prandial/fasting blood glucose concentration during the intervention (timing not defined) for women with GDM between the energy restricted diet and no energy restricted diet group (MD 0.21 mmol/L, 95% CI -0.58 to -0.99; two trials, 311 women; *low-quality evidence*) (Han 2017).

10.2.2 High unsaturated fat diet versus low unsaturated fat diet with matching calories: The evidence suggested a small but elevated fasting glucose concentration during the intervention at 38 weeks' gestation for women with GDM in the high unsaturated fat diet group compared to the low unsaturated fat diet with matching calories group (MD 0.50 mmol/L, 95% CI 0.30 to 0.70; one trial, 24 women; *low-quality evidence*) (Han 2017).

10.3 Glycaemic control during the treatment: post-prandial

10.3.1 Energy restricted diet versus no energy restricted diet: There was no clear difference in one-hour post-prandial glucose concentration for women with GDM between the energy restricted diet and no energy restricted diet group (MD -0.25 mmol/L, 95% CI -0.68 to -0.18; one trial, 299 women; *low-quality evidence*) (Han 2017).

10.3.2 High unsaturated fat diet versus low unsaturated fat diet with matching calories: The evidence suggested higher post-prandial glucose concentration (no post-prandial time given) during the intervention at 38 weeks' gestation for women with GDM in the high unsaturated fat diet group compared to the low unsaturated fat diet with matching calories group (MD 0.90 mmol/L, 95% CI 0.58 to 1.22; one trial, 25 women; *low-quality evidence*) (Han 2017).

10.4 Glycaemic control during treatment: HbA1c

10.4.1 Metformin versus glibenclamide: There was no clear difference in HbA1c in the third trimester of the pregnancy for women with GDM between the metformin and glibenclamide group (SMD -0.12, 95% CI -0.39 to 0.16; one trial, 200 women; *low-quality evidence*) (Brown 2017a).

10.4.2 High unsaturated fat diet versus low unsaturated fat diet with matching calories: The evidence suggested higher HbA1c results during the intervention at 38 weeks' gestation for women with GDM in the high unsaturated fat diet group compared to the low unsaturated fat diet with matching calories group (MD 0.40 %, 95% CI 0.32 to 0.48; one trial, 25 women; *low-quality evidence*) (Han 2017).

10.5 Glycaemic control during the treatment: 24 hour mean plasma glucose

10.5.1 Energy restricted diet versus no energy restricted diet: There was no clear difference in the 24 hour mean plasma glucose concentration during the intervention for women with GDM between the energy restricted diet and no energy restricted diet group (MD 0.10 mmol/L, 95% CI -0.82 to 1.02; one trial, 12 women; *low-quality evidence*) (Han 2017).

10.6 Glycaemic control at the end of treatment: Fasting

10.6.1 Oral antidiabetic agents versus placebo: The evidence suggested a reduction in fasting capillary glucose concentration (taken at the last three antenatal visits) for women with GDM in the oral

antidiabetic drug glibenclamide group compared to the placebo group (MD -3.0 mg/dL, 95% CI -5.13 to -0.87; one trial, 375 women; *low-quality evidence*) (Brown 2017a).

10.6.2 Metformin versus glibenclamide: The evidence suggested an increase in fasting blood glucose concentration at the end of treatment for women with GDM in the metformin group compared to the glibenclamide group (SMD 0.19 mmol/L, 95% CI 0.02 to 0.37; three trials, 508 women; *low-quality evidence*) (Brown 2017a).

10.6.3 Myo-inositol versus placebo: The evidence suggested a reduction in fasting blood glucose concentration at the end of treatment (with OGTT) for women with GDM in the myo-inositol group compared to the placebo 400 mcg folic acid orally per day and exercise and dietary advice group (MD -0.47 mmol/L, 95% CI -0.59 to -0.35; two trials, 142 women; *moderate-quality evidence)* (Brown 2016a).

10.6.4 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference in fasting plasma glucose concentration at the end of treatment for women with GDM between the low-moderate GI diet and moderate-high GI diet group (MD -0.15 mmol/L, 95% CI -0.55 to 0.25; one trial, 83 women; *very low-quality evidence*) (Han 2017).

10.6.5 Energy restricted diet versus no energy restricted diet: The evidence suggested a reduction in fasting blood glucose concentration at the end of treatment for women with GDM in the energy restricted diet group compared to the no energy restricted diet group (MD -0.23 mmol/L, 95% CI -0.44 to -0.03; two trials, 311 women; *low-quality evidence*) (Han 2017).

10.6.6 DASH diet versus control diet with matching macronutrient contents: The evidence suggested a reduction in fasting blood glucose concentration at the end of treatment for women with GDM in the DASH diet group compared to the diet with matching macronutrient contents group (MD -0.42 mmol/L, 95% CI -0.53 to -0.32; two trials, 66 women; *moderate-quality evidence*) (Han 2017).

10.6.7 Low carbohydrate diet versus high-carbohydrate diet: There was no clear difference in fasting blood glucose concentration at the end of treatment for women with GDM between the low carbohydrate diet and high-carbohydrate diet group (MD 5.00 mg/dL, 95% CI -0.01 to 10.01; one trial, 30 women; *very low-quality evidence*) (Han 2017).

10.6.8 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference in fasting blood glucose concentration at the end of treatment for women with

GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (MD 0.18 mmol/L, 95% CI -0.17 to 0.53; one trial, 84 women; *low-quality evidenc*e) (Han 2017).

10.6.9 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference in fasting blood glucose concentration at the end of treatment for women with GDM between the diet recommendation + diet-related behavioural advice and diet recommendation only group (MD 0.0 mg/dL, 95% CI -4.25 to 4.25; one trial, 99 women; *very low-quality evidence*) (Han 2017).

10.6.10 Soy protein-enriched diet versus no soy protein diet: The evidence suggested a reduction in fasting plasma glucose concentration at the end of treatment for women with GDM in the soy protein-enriched diet group compared to the no soy protein diet group (MD -10.60 mg/dL, 95% CI -15.37 to -5.83; one trial, 68 women; *very low-quality evidence*) (Han 2017).

10.6.11 Exercise versus control: The evidence suggested a reduction in fasting plasma glucose concentration at the end of treatment for women with GDM in the exercise group compared to the control group (average SMD -0.59, 95% CI -1.07 to -0.11; four trials, 363 women; I^2 = 73%; *low-quality evidence*) (Brown 2017c).

10.7 Glycaemic control at the end of treatment: One-hour post-prandial

10.7.1 Myo-inositol versus placebo: The evidence suggested a reduction in one-hour post-prandial blood glucose concentration (with OGTT) at the end of treatment for women with GDM in the myo-inositol group compared to the placebo group (MD -0.90 mmol/L, 95% CI -1.73 to -0.07; one trial, 73 women; *moderate-quality of evidence*) (Brown 2016a).

10.7.2 Energy restricted diet versus no energy restricted diet: The evidence suggested a reduction in one-hour post-prandial blood glucose concentration at the end of treatment for women with GDM in the energy restricted diet group compared to the no energy restricted diet group (MD -0.51 mmol/L, 95% CI -0.89 to -0.13; one trial, 299 women; *low quality evidence*) (Han 2017).

10.7.3 Lifestyle intervention versus usual care or diet alone: The evidence suggested a reduction post-prandial blood glucose concentration at the end of treatment (timing reported as one-hour post-prandial in two trials; two-hours in two trials and one trial did not define the timing) for women with GDM

in the lifestyle intervention group compared to the usual care or diet alone group (average MD -27.11 mg/dL, 95% CI -44.62 to -9.61; four trials, 588 women; *very low-quality evidence*) (Brown 2017b).

10.8 Glycaemic control at the end of treatment: Two-hours post-prandial

10.8.1 Metformin versus glibenclamide: There was no clear difference in the two-hour post-prandial blood glucose concentration (measured after dinner, where specified) for women with GDM between the metformin and glibenclamide group (SMD 0.16, 95% CI -0.01 to 0.34; three trials, 508 women; *low-quality evidence*) (Brown 2017a).

10.8.2 Myo-inositol versus placebo: There was no clear difference in two-hour post-prandial blood glucose concentration at the end of treatment (with OGTT) for women with GDM between the myo-inositol and the placebo group (MD -0.70 mmol/L, 95% CI -1.46 to 0.06; one trial, 73 women; *low-quality evidence*) (Brown 2016a).

10.8.3 Low-moderate GI diet versus moderate-high GI diet: The evidence suggested a reduction in two-hour post-prandial blood glucose concentration at the end of treatment for women with GDM in the low-moderate GI diet group compared to the moderate-high GI diet group (MD -0.71 mmol/L, 95% CI -1.21 to -0.21; one trial, 83 women; *very low-quality evidence*) (Han 2017).

10.8.4 Low carbohydrate diet versus high-carbohydrate diet: There was no clear difference in two-hour post-prandial blood glucose concentration (measured after breakfast) at the end of treatment for women with GDM between the low carbohydrate diet and high-carbohydrate diet group (MD 6.00 mg/dL, 95% CI -1.47 to 13.47; one trial, 30 women; *very low-quality evidence*) (Han 2017).

10.8.5 Low carbohydrate diet versus high-carbohydrate diet: There was no clear difference in two-hour post-prandial blood glucose concentration (measured after lunch) at the end of treatment for women with GDM between the low carbohydrate diet and high-carbohydrate diet group (MD 3.00 mg/dL, 95% CI -2.77 to 8.77; one trial, 30 women; *very low-quality evidence*) (Han 2017).

10.8.6 Low carbohydrate diet versus high-carbohydrate diet: There was no clear difference in two hours post-prandial blood glucose concentration (measured after dinner) at the end of treatment for women with GDM between the low carbohydrate diet and high-carbohydrate diet group (MD 6.00 mg/dL, 95% CI -1.47 to 13.47; one trial, 30 women; *very low-quality evidence*) (Han 2017).

10.8.7 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference in the two-hour post-prandial blood glucose concentration at the end of treatment for women with GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (MD -0.02 mmol/L, 95% CI -0.29 to 0.25; one trial, 84 women; *low-quality evidence*) (Han 2017).

10.9 Glycaemic control at the end of treatment: Post-prandial timing not defined

10.9.1 Diet recommendation + diet-related behavioural advice versus diet recommendation only: The evidence suggested a reduction in post-prandial blood glucose concentration at the end of treatment (timing not defined) for women with GDM in the diet recommendation + diet-related behavioural advice compared to the diet recommendation only group (MD -9.30 mg/dL, 95% CI -15.58 to -3.02; one trial, 99 women; *very low-quality evidence*) (Han 2017).

10.9.2 Exercise versus control: The evidence suggested a reduction in post- prandial blood glucose concentration at the end of treatment (timing not defined) for women with GDM in the exercise group compared to the control group (average SMD -0.85, 95% CI -1.15 to -0.55; three trials, 344 women; *moderate-quality evidence*) (Brown 2017c).

10.9.3 Exercise versus control: The evidence suggested a reduction in the OGTT result for women with GDM at the end of treatment in the exercise group compared with the control group (MD -81.60 mg/dl, 95% CI -96.03 to -67.17; one trial, 19 women; *low-quality evidence*) (Brown 2017c).

10.10 Glycaemic control at the *end* of treatment: mean plasma glucose

10.10.1 Energy restricted diet versus no energy restricted diet: The evidence suggested a reduction in 24-hour mean plasma glucose concentration for women with GDM in the energy restricted diet group compared to the no energy restricted diet group (MD -1.30 mmol/L, 95% CI -2.25 to -0.35; one trial, 12 women; *low-quality evidence*) (Han 2017).

10.10.2 Exercise versus control: The evidence suggested a higher mean plasma glucose concentration for women with GDM in the exercise group compared to the control group (MD 0.28 mmol/L, 95% CI 0.04 to 0.52; one trial, 34 women; *very low-quality evidence*) (Brown 2017c). It is unclear if a difference of 0.28 mmol/L is of clinical significance.

10.11 Glycaemic control at the *end* of treatment: HbA1c

10.11.1 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for HbA1c concentration for women with GDM between the low-moderate GI diet and moderate-high GI diet group (MD 0.01 %, 95% CI -0.18 to 0.20; one trial, 83 women; *very low-quality evidence*) (Han 2017).

10.11.2 DASH diet versus control diet with matching macronutrient contents: The evidence suggested a reduction in HbA1c concentration at the end of treatment for women with GDM in the DASH diet group compared to the control diet with matching macronutrient contents group (MD -0.25 %, 95% CI -0.76 to 0.26; one trial, 34 women; *moderate-quality evidence*) (Han 2017).

10.11.3 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference in HbA1c concentration at the end of treatment for women with GDM between the diet recommendation + diet-related behavioural advice and diet recommendation only group (MD -0.10 %, 95% CI -0.28 to 0.08; one trial, 99 women; *very low-quality evidence*) (Han 2017).

10.11.4 Lifestyle intervention versus usual care or diet alone: The evidence suggested a reduction in HbA1c concentration at the end of treatment for women with GDM in the lifestyle intervention group compared to the usual care or diet alone group (average MD -0.33 mmol/mol, 95% CI -0.47 to -0.19; six trials, 532 women; *very low-quality evidence*) (Brown 2017b).

10.11.5 Exercise versus control: There was no clear difference in HbA1c concentration at the end of treatment for women with GDM between the exercise and control group (MD -0.43 mmol/mol, 95% CI -0.51 to -0.35; two trials, 320 women; *high-quality evidence*) (Brown 2017c).

10.12 Glycaemic control *during/at the end* of treatment: Fasting

10.12.1 Energy restricted diet versus no energy restricted diet: There was no clear difference in the fasting blood glucose concentration at the end of treatment for women with GDM between the energy restricted diet and no energy restricted diet group (MD 0.10 mmol/L, 95% CI -0.18 to -0.38; one trial, 117 women; *very low-quality evidence*) (Han 2017).

10.12.2 Lifestyle intervention versus usual care or diet alone: There was no clear difference in the fasting blood glucose concentration during/at the end of treatment for women with GDM between the

lifestyle intervention and usual care or diet alone group (average MD -3.10 mg/dL, 95% CI -7.01 to 0.81; six trials, 853 women; *very low-quality evidence*). Data from one trial reported on median and range for postnatal fasting blood glucose concentration, which could not be included in the meta-analysis, however there was no clear evidence of a difference between the intervention and control group (Brown 2017b).

10.13 Glycaemic control *during/at the end* of treatment: Mean plasma glucose

10.13.1 Energy restricted diet versus no energy restricted diet: There was no clear difference in the mean plasma glucose concentration during/at the end of treatment for women with GDM between the energy restricted diet and no energy restricted diet group (MD 0.10 mmol/L, 95% CI -0.34 to -0.54; one trial, 117 women; *very low-quality evidence*) (Han 2017).

10.13.2 High-fibre diet versus standard-fibre diet: There was no clear difference in the mean plasma glucose concentration during/at the end of treatment for women with GDM between high-fibre diet and standard-fibre diet (MD 0.0 mmol/L, 95% CI -8.26 to 8.26; one trial, 22 women; *very low-quality evidence*) (Han 2017).

10.14 Glycaemic control *during/at the end* of treatment: HbA1c

10.14.1 Energy restricted diet versus no energy restricted diet: There was no clear difference in mean HbA1c at the end of treatment for women with GDM between the energy restricted diet and no energy restricted diet group (MD -0.20 %, 95% CI -0.64 to -0.24; one trial, 117 women; *low-quality evidence*) (Han 2017).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence suggested a benefit by a reduction in fasting blood glucose concentration and one-hour post-prandial blood glucose concentration at the end of treatment for women with GDM who were treated with myo-inositol compared to placebo; a reduction in post-prandial (timing not defined) blood glucose concentration at the end of treatment for women with GDM who were treated with exercise compared to control or a reduction in fasting blood glucose and mean HbA1c at the end of treatment for women with GDM who were treated with the DASH diet compared to the control diet with matching macronutrient contents.

Ineffective interventions: high-quality evidence of lack of effectiveness

- *High-quality* evidence showed no clear difference for HbA1c at the end treatment for women with GDM who were treated with exercise versus control.

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit by a reduction in fasting blood glucose concentration at the end of treatment for women with GDM who were treated with glibenclamide compared to placebo; energy restricted diet compared to the no energy restricted diet; or exercise compared to control; a reduction in one-hour post-prandial blood glucose concentration and 24-hour mean plasma glucose concentration at the end of treatment for women with GDM who were treated with the energy restricted diet compared to no energy restricted diet or a reduction in OGTT at the end of treatment for women with GDM who were treated with exercise compared to control.
- *Very low-quality* suggested a benefit by a reduction in fasting blood glucose concentration at the end of treatment for women with GDM who were treated with soy protein-enriched diet compared to no soy protein diet ; a *reduction* in one-hour post-prandial blood glucose concentration at the end of treatment for women with GDM who were treated with lifestyle interventions compared to usual care or diet alone; a *reduction* in two-hour post-prandial blood glucose concentration at the end of treatment for women with GDM who were treated with the low-moderate GI diet compared to moderate-high GI diet; a reduction in post-prandial (undefined) blood glucose concentration at the end of treatment for women with GDM who were treated with diet recommendation + diet-related behavioural advice compared to diet recommendation only or a reduction in mean HbA1c at the end of treatment for women with GDM who were treated with lifestyle interventions compared usual care or diet alone.
- *Low-quality* evidence suggested harm by an increased fasting and post-prandial (undefined) blood glucose concentration and HbA1c during treatment at 38 weeks' gestation for women with GDM who were treated with a high unsaturated fat diet compared to a low unsaturated fat diet with matching calories or an increase in fasting blood glucose concentration at the end of treatment for women with GDM who were treated with metformin compared to glibenclamide. *Very low*-quality evidence suggested harm by an increased mean plasma glucose concentration at the end of treatment for women with GDM who were treated with exercise compared to control.
- *Low-quality* evidence showed no clear difference in fasting, one-hour post-prandial blood glucose concentration and 24-hour mean plasma glucose concentration during (not defined) treatment and mean HbA1c during/at the end of treatment for women with GDM who were treated with the energy restricted diet versus no energy restricted diet ; no clear difference for HbA1c during treatment (not defined) for women with GDM who were treated with metformin versus glibenclamide; no clear difference in fasting blood glucose concentration at the end of treatment for women with GDM who were treated with high unsaturated fat diet versus low unsaturated fat diet with matching calories or no clear difference in two hours post-prandial blood glucose concentration at the end of treatment for women with GDM who were treated with metformin versus glibenclamide (after dinner); or with myo-inositol versus placebo.
- *Very low-quality* evidence showed no clear difference for glycaemic control (not defined) for women with GDM who were treated with a low-GI diet versus high-fibre moderate-GI diet; no clear difference in fasting blood glucose concentration at the end of treatment for women with GDM who were treated with low-moderate GI diet compared to moderate-high GI diet; or low carbohydrate diet compared to high-carbohydrate diet; or Diet recommendation + diet-related behavioural advice compared to diet recommendation only; no clear difference in two hours post-prandial blood glucose concentration at the end of treatment for women with GDM who were treated with a high unsaturated fat diet versus low unsaturated fat diet with matching calories; or low carbohydrate diet compared to a high-carbohydrate diet after breakfast, lunch or dinner; no clear difference for mean HbA1 at the end of treatment for women with GDM who were treated with a low-moderate GI diet compared to a moderate-high GI diet; or Diet

recommendation + diet-related behavioural advice compared to diet recommendation only; no clear difference in fasting blood glucose concentration at the during/at the end of treatment for women with GDM who were treated with an energy restricted diet compared to a no energy restricted diet; or lifestyle intervention compared usual care or diet alone or no clear difference for mean plasma glucose during/at the end of treatment for women with GDM who were treated with an energy restricted diet compared to no energy restricted diet; or with a high-fibre diet compared to a standard-fibre diet.

11.0 Weight gain in pregnancy

Weight gain in pregnancy was reported as an outcome in six reviews (Brown 2016a; Brown 2017a; Brown 2017b; Brown 2017c; Han 2012; Han 2017) (Table 2.11; Table 2.19). It was not clear from the reviews regarding the timing of weight gain in pregnancy. The quality of the evidence ranged from *moderate- to very low-quality.*

11.1 Oral antidiabetic agents versus placebo: There was no difference in weight gain in pregnancy for women with GDM between glibenclamide and placebo group (MD 0.0 kg, 95% CI -0.96 to 0.96; one trial, 375 women; *low-quality evidence*) (Brown 2017a).

11.2 Metformin versus glibenclamide: The evidence suggested reduced weight gain in pregnancy for women with GDM in the metformin group compared to the glibenclamide group (MD -2.06 kg, 95% CI -3.98 to -0.14; one trial, 200 women; *very low-quality evidence*) (Brown 2017a).

11.3 Glibenclamide versus acarbose: There was no clear difference in weight gain in pregnancy for women with GDM between the glibenclamide and acarbose group (MD -0.60 kg, 95% CI -3.13 to -1.93; one trial, 43 women; *very low-quality evidence*) (Brown 2017a).

11.4 Myo-inositol versus placebo: There was no clear difference for the risk of weight gain in pregnancy for women with GDM between the myo-inositol and the placebo group (MD -0.50 kg, 95% CI -3.35 to 2.25; one trial, 69 women; *very low-quality evidence*) (Brown 2016a).

11.5 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference in weight gain in pregnancy for women between the low-moderate GI diet and moderate-high GI diet group (MD -0.47 kg, 95% CI -2.18 to 1.24; one trial, 83 women; *very low-quality evidence*) (Han 2017).

11.6 Energy restricted diet versus no energy restricted diet: There was no clear difference in weight gain in pregnancy for women between the energy restricted diet and no energy restricted diet group (MD 1.88 kg, 95% CI -1.96 to 5.72; one trial, 117 women; *very low-quality evidence*) (Han 2017).

11.7 DASH diet versus control diet with matching macronutrient contents: There was showed no clear difference in weight gain in pregnancy for women with GDM between the DASH diet and control diet with matching macronutrient contents group (MD -2.88 kg, 95% CI -8.48 to 2.71; two trials, 66 women; *moderate-quality evidence*) (Han 2017).

11.8 Low-carbohydrate diet versus high-carbohydrate diet: The evidence suggested less weight gain in pregnancy for women with GDM in the low-carbohydrate diet group compared to the high-carbohydrate diet group (MD -0.90 kg, 95% CI -1.60 to -0.20; one trial, 145 women; *low-quality evidence*) (Han 2017).

11.9 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference in weight gain in pregnancy for women with GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (MD -1.98 kg, 95% CI -4.32 to 0.36; one trial, 84 women; *low-quality evidence*) (Han 2017).

11.10 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference in weight gain in pregnancy for women with GDM between the low-GI diet and high-fibre moderate-GI diet group (MD -1.20 kg, 95% CI -3.43 to 1.03; one trial, 87 women; *very low-quality evidence*) (Han 2017).

11.11 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference in weight gain in pregnancy for women with GDM between the diet recommendation + diet-related behavioural advice and diet recommendation only group (MD -0.10 kg, 95% CI -4.91 to 4.71; one trial, 99 women; *very low-quality evidence*) (Han 2017).

11.12 Soy protein-enriched diet versus no soy protein diet: There was no clear difference in weight gain in pregnancy for women with GDM between the soy protein-enriched diet and no soy protein diet group (MD 3.50 kg, 95% CI -1.47 to 8.47; one trial, 68 women; *very low-quality evidence*) (Han 2017).

11.13 High-fibre diet versus standard-fibre diet: There was no clear difference in weight gain in pregnancy for women with GDM between high-fibre diet and standard-fibre diet (MD 2.40 kg, 95% CI -2.20 to 7.00; one trial, 22 women; *very low-quality evidence*) (Han 2017).

11.14 Ethnic specific diet versus standard healthy diet: There was no clear difference in weight gain in pregnancy for women with GDM between the ethnic specific diet and standard healthy diet group (MD -2.20 kg, 95% CI -7.24 to 2.84; one trial, 20 women; *very low-quality evidence*) (Han 2017).

11.15 Lifestyle intervention versus usual care or diet alone: The evidence suggested less weight gain in pregnancy at the end of the intervention for women with GDM in the lifestyle intervention group compared to the usual care or diet alone group (average MD -1.30 kg, 95% CI -2.26 to -0.35; four trials, 2930 women; *moderate-quality evidence*) (Brown 2017b).

11.16 Exercise versus control: There was no clear difference in weight gain in pregnancy for women with GDM between the exercise and control group (MD -0.34 kg, 95% CI -1.25 to 0.58; two trials, 104 women; *low-quality evidence*) (Brown 2017c). The increase in weight differs substantially between the two trials. There was no clear explanation for this.

11.17 Intensive management versus routine care: There was no clear difference in weight gain in pregnancy for women with GDM between the intensive management and routine care group (MD -0.63 kg, 95% CI -3.07 to 1.81; two trials, 426 women; *very low-quality evidence*) (Han 2012).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence suggested a benefit by reduced weight gain in pregnancy for women who were treated with lifestyle intervention compared to usual care or diet alone.

Probably no difference between interventions: direction of effect suggests benefit, but more evidence needed

- *Moderate-quality* evidence showed no clear difference for weight gain in pregnancy for women with GDM who were treated DASH diet and control diet with matching macronutrient contents, suggesting a similar risk for both diet interventions for weight gain in pregnancy.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit by reduced weight gain in pregnancy for women with GDM who were treated with the low-carbohydrate diet compared to high-carbohydrate diet.
- *Low-quality* evidence showed no clear difference in weight gain in pregnancy for women with GDM who were treated with glibenclamide versus placebo; with a high unsaturated fat diet versus low unsaturated fat diet with matching calories; or exercise versus control.
- *Very low-quality* evidence suggested a benefit by reduced weight gain in pregnancy for women with GDM who were treated with metformin compared to glibenclamide.
- *Very low-quality* evidence showed no clear difference in weight gain in pregnancy for women with GDM who were treated with glibenclamide versus acarbose; myo-inositol versus placebo; low-moderate GI diet versus moderate-high GI diet; energy restricted diet versus no energy restricted diet; low-GI diet versus high-fibre moderate-GI diet; diet recommendation + diet-

related behavioural advice versus diet recommendation only; soy protein-enriched diet versus no soy protein diet; with high-fibre diet versus standard-fibre diet; with ethnic specific diet versus standard healthy diet; or intensive management versus routine care.

12.0 Other measures of weight gain in pregnancy (not pre-specified for this overview)

Three reviews (Brown 2016a; Brown 2017c; Han 2017) reported on the outcome of BMI during or at the end of treatment. One review reported on excessive weight gain in pregnancy (Brown 2017c) (Table 2.11; Table 2.19). We considered these as alternate measures for weight gain in pregnancy although we had not pre-specified them as outcomes in our protocol. The quality of the evidence ranged from *moderate- to very low-quality.* There was no clear evidence of a difference for other measures of weight gain in pregnancy for any of the comparisons reporting this outcome.

12.1 Myo-inositol versus placebo: The evidence suggested a reduction of BMI during pregnancy for women with GDM in the myo-inositol group compared to the placebo 400 mcg folic acid orally per day and exercise and dietary advice group (MD -1.50 kg/m^2, 95% CI -2.35 to -0.65; one trial, 73 women; *moderate-quality evidence*) (Brown 2016a).

12.2 DASH diet versus control diet with matching macronutrient contents: There was no clear difference of BMI at the end of the pregnancy for women with GDM between the DASH diet and control diet with matching macronutrient contents group (MD -0.83 in kg/m^2, 95% CI -3.76 to 2.11; two trials, 66 women; *moderate-quality evidence*) (Han 2017).

12.3 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference of BMI at the end of the pregnancy for women with GDM between the diet recommendation + diet-related behavioural advice and diet recommendation only group (MD -0.0 kg/m^2, 95% CI -1.75 to 1.75; one trial, 99 women; *very low-quality evidence*) (Han 2017).

12.4 Soy protein-enriched diet versus no soy protein diet: There was no clear difference of BMI at the end of the pregnancy for women with GDM in the soy protein-enriched diet and no soy protein diet group (MD 0.60 kg/m^2, 95% CI -1.43 to 2.63; one trial, 68 women; *very low-quality evidence*) (Han 2017).

12.5 Exercise versus control: There was no clear difference for excessive weight gain in pregnancy for women with GDM between the exercise and control group (RR 0.90, 95% CI 0.47 to 1.72; one trial, 79 women; *very low-quality evidence*) (Brown 2017c).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence suggested a benefit by a reduction of BMI during pregnancy for women with GDM who were treated with myo-inositol compared to placebo.

Probably no difference between interventions: direction of effect suggests benefit, but more evidence needed

- *Moderate-quality* evidence showed no clear difference for BMI at the end of the pregnancy for women with GDM who were treated DASH diet and control diet with matching macronutrient contents, suggesting a similar risk for both diet interventions for weight gain in pregnancy.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence showed no clear difference in excessive weight gain in pregnancy for women with GDM who were treated with exercise versus control and no clear evidence of a difference in BMI at the end of the pregnancy for women with GDM who were treated with diet recommendation + diet-related behavioural advice versus diet recommendation only; or soy protein-enriched diet versus no soy protein.

13.0 Adherence to the intervention

Adherence to the intervention was reported as an outcome by two reviews (Han 2017; Brown 2017c) (Table 2.11; Table 2.19). The quality of the evidence ranged from *low- to very low-quality.* There was no clear evidence of a difference for adherence to the intervention for any of the comparisons reporting this outcome.

13.1 Low-carbohydrate diet versus high-carbohydrate diet: There was no clear difference for women with GDM who fully adhered to the intervention (adherence not defined) between the low-carbohydrate and high-carbohydrate diet group (RR 1.09, 95% CI 0.73 to 1.62; one trial, 30 women; *low-quality evidence*) (Han 2017).

13.2 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for women with GDM who fully adhered to the intervention (assessed by a 24-hour recall when women were attending their dietitian appointment) between the low-GI diet and high-fibre moderate-GI diet group (RR 0.84, 95% CI 0.64 to 1.11; one trial, 92 women; *very low-quality evidence*) (Han 2017).

13.3 Ethnic specific diet versus standard healthy diet: There was no clear difference for women with GDM who fully adhered to the intervention between the ethnic specific diet and standard healthy diet group (RR 3.50, 95% CI 0.95 to 12.90; one trial, 20 women; *very low-quality evidence*) (Han 2017). Adherence to the intervention was defined in the review as: " adherence to the dietary intervention was measured using a 24-hour food intake recall method; women with an intake of more than 20% higher

than prescribed received a score of 0; those with an intake of 10% to 20% higher received a score of 1; and women with intake consistent with the plan or up to 10% lower received a score of 2. 'Good adherence' was defined as women being scored a 1 or 2.

13.4 Exercise versus control: There was no clear difference for women with GDM who fully adhered to the intervention between the exercise and the control group (RR 1.00, 95% CI 0.83 to 1.21; one trial, 19 women; *low-quality evidence*) (Brown 2017c).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for adherence to the intervention for women with GDM who were treated with a low-carbohydrate diet versus high-carbohydrate diet; or exercise versus control.
- *Very low-quality* evidence showed no clear difference for adherence to the intervention for women with GDM who were treated with a low-GI diet versus high-fibre moderate-GI diet; or with an ethnic specific diet versus standard healthy diet for adherence to the intervention.

14.0. Induction of labour

Induction of labour was reported as an outcome by five reviews (Brown 2017a; Han 2017; Brown 2017b; Brown 2017c; Han 2012) (Table 2.; Table 2.18). The quality of the evidence ranged from *high- to very low-quality.*

14.1 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of induction of labour for women with GDM between the glibenclamide and placebo group (RR 1.18, 95% CI 0.79 to 1.76; one trial, 375 women; *very low-quality evidence*) (Brown 2017a).

14.2 Metformin versus glibenclamide: There was no clear difference for the risk of induction of labour for women with GDM between the metformin and glibenclamide group (RR 0.81, 95% CI 0.61 to 1.07; one trial, 159 women; *low-quality evidence*) (Brown 2017a).

14.3 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the risk of induction of labour for women with GDM between the low-moderate GI diet and moderate-high GI diet group (RR 0.88, 95% CI 0.33 to 2.34; one trial, 63 women; *low-quality evidence*) *(*Han 2017).

14.4 Energy restricted diet versus no energy restricted diet: There was no clear difference for the risk of induction of labour for women with GDM between the energy restricted diet and no energy

restricted diet group (RR 1.02, 95% CI 0.68 to 1.53; one trial, 114 women; *low-quality evidence*) *(*Han 2017).

14.5 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of induction of labour for women with GDM between the lifestyle intervention and usual care or diet alone group (average RR 1.20, 95% CI 0.99 to 1.46; four trials, 2699 women; *high-quality evidence*) (Brown 2017b).

14.6 Exercise versus control: There was no clear difference for the risk of induction of labour for women with GDM (RR 1.38, 95% CI 0.71 to 2.68; one trial, 40 women; *low quality evidence*) (Brown 2017c).

14.7 Intensive management versus routine care: The evidence suggested an increased risk of induction of labour for women with GDM in the intensive management group compared to the routine care group (RR 17.69, 95% CI 1.03 to 304.09; one trial, 83 women; *very low-quality evidence*) (Han 2012). There were six events of induction of labour for women with GDM in the intensive management group but no events in the control group.

Summary

Ineffective interventions: high-quality evidence of lack of effectiveness

- *High-quality* evidence showed no clear difference for the risk of induction of labour for women with GDM who were treated with lifestyle intervention versus usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence suggested harm by an increased risk of induction in labour for women with GDM who were treated with intensive management compared to the routine care.
- *Low-quality* evidence showed no clear difference for the risk of induction of labour for women with GDM who were treated with metformin versus glibenclamide; low-moderate GI diet versus moderate-high GI diet; energy restricted diet versus no energy restricted diet; or exercise versus control.
- *Very low-quality* evidence showed no clear difference for the risk of induction of labour for women with GDM who were treated with glibenclamide versus placebo.

15.0 Placental abruption

Placental abruption was reported as an outcome in one review (Han 2017) (Table 2.11; Table 2.19). The quality of the evidence was *low-quality.* There was no clear evidence of a difference for the risk of placental abruption for either of the comparisons reporting this outcome.

15.1 DASH diet versus control diet with matching macronutrient contents: There was no clear difference for the risk of placental abruption for women with GDM between the DASH diet and control diet with matching macronutrient contents group (RR 3.00, 95% CI 0.13 to 70.73; one trial, 58 women; *low-quality evidence*) (Han 2017).

15.2 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for the risk of placental abruption for women with GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (RR not estimable; one trial, 27 women; *low-quality evidence*) (Han 2017). There were no events of placental abruption in either group.

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the risk of placental abruption for women with GDM who were treated with the DASH diet versus control diet with matching macronutrient contents; or high unsaturated fat diet versus low unsaturated fat diet with matching calories.

16.0 Postpartum haemorrhage (as defined in the reviews)

Postpartum haemorrhage was reported as an outcome by two reviews (Brown 2017b; Han 2017) (Table 2.11; Table 2.19). Neither review defined postpartum haemorrhage. The quality of the evidence ranged from *low- to very low- quality.* There was no clear evidence of a difference for the risk of postpartum haemorrhage for either of the comparisons reporting this outcome.

16.1 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the risk of postpartum haemorrhage for women with GDM between the low-moderate GI diet and moderate-high GI diet group (RR 1.02, 95% CI 0.15 to 6.93; one trial, 83 women; *very low-quality evidence*) (Han 2017).

16.2 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of postpartum haemorrhage for women with GDM between the lifestyle intervention and usual care or diet alone group (average RR 0.61, 95% CI 0.20 to 1.89; two trials, 1165 women; *low-quality evidence*) (Brown 2017b).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

Summary

- *Low-quality* evidence showed no clear difference for the risk of postpartum haemorrhage (not defined) for women with GDM who were treated with lifestyle intervention versus usual care or diet alone.
- *Very low-quality* evidence showed no clear difference for the risk of postpartum haemorrhage (not defined) for women with GDM who were treated with low-moderate GI diet versus moderate-high GI diet.

17.0 Postpartum infection

Postpartum infection was reported as an outcome by two reviews (Brown 2017b; Han 2017) (Table 2.11; Table 2.19). The quality of the evidence ranged from *moderate- to very low- quality.* There was no clear evidence of a difference for the risk of postpartum infection for either of the comparisons reporting this outcome.

Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the risk of postpartum infection for women with GDM between the low-moderate GI diet and moderate-high GI diet group (RR 0.34, 95% CI 0.01 to 8.14; one trial, 83 women; *very low-quality evidence*) (Han 2017).

Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of postpartum infection for women between the lifestyle intervention and usual care or diet alone group (RR 0.61, 95% CI 0.34 to 1.10; one trial, 1000 women; *moderate-quality evidence*) (Brown 2017b).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed no clear difference for the risk of postpartum infection for women with GDM who were treated with lifestyle intervention versus usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence showed no clear difference for the risk of postpartum infection for women with GDM who were treated with low-moderate GI diet versus moderate-high GI diet.

18.0 Perineal trauma/tearing

Perineal trauma/tearing was reported as an outcome by two reviews (Brown 2017a; Brown 2017b) (Table 2.8; Table 2.19). The quality of the evidence ranged from *moderate- to very low- quality.* There was no clear evidence of a difference for the risk of perineal trauma/tearing for any of the comparisons reporting this outcome.

18.1 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of perineal trauma/tearing (defined as third to fourth degree tear) for women with GDM between glibenclamide and placebo group (RR 0.98, 95% CI 0.06 to 15.62; one trial, 375 women; *very low-quality evidence*) (Brown 2017a).

18.2 Metformin versus glibenclamide: There was no clear difference for the risk of perineal trauma/tearing (defined as third and fourth degree perineal tearing) for women with GDM between the metformin and glibenclamide group (RR 1.67, 95% CI 0.22 to 12.52; two trials, 308 women; *low-quality evidence*) (Brown 2017a).

18.3 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of perineal trauma/tearing (not defined) for women with GDM between the lifestyle intervention and usual care or diet alone group (RR 1.04, 95% CI 0.93 to 1.18; one trial, 1000 women; *moderate-quality evidence*) (Brown 2017b).

Summary

Probably no difference between interventions: Direction of the effect suggested ineffective intervention: moderate quality evidence.

- *Moderate-quality* evidence showed no clear difference for the risk of perineal trauma/tearing for women with GDM who were treated with lifestyle intervention versus usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the risk of perineal trauma/tearing for women with GDM who were treated with metformin versus glibenclamide.
- *Very low-quality* evidence showed no clear difference for the risk of perineal trauma/tearing for women with GDM who were treated with glibenclamide versus placebo.

19.0 Breastfeeding at discharge, six weeks postpartum, six months or longer

Breastfeeding was reported as an outcome by one review (Brown 2017b). Data were reported at discharge, at six weeks postpartum and six months postpartum. The quality of the evidence ranged from *moderate - to very low- quality.* There was no clear evidence of a difference between groups for breastfeeding at any of the time points reported for this comparison.

19.1 Breastfeeding at discharge

19.1.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for breastfeeding at discharge for women with GDM between the lifestyle intervention and usual care or diet alone group (RR 1.04, 95% CI 0.99 to 1.10; one trial, 1000 women; *moderate-quality evidence*) (Brown 2017b).

19.1.2 Breastfeeding at six weeks post-partum

Lifestyle intervention versus usual care or diet alone: There was no clear difference for breastfeeding at six weeks post-partum for women with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.97, 95% CI 0.87 to 1.07; one trial, 188 women; *very low-quality evidence*) (Brown 2017b).

19.1.3 Breastfeeding at six months postpartum or longer

Lifestyle intervention versus usual care or diet alone: There was no clear difference for breastfeeding at six months post-partum for women with GDM between the lifestyle intervention and usual care or diet alone group (RR 1.31, 95% CI 0.99 to 1.74; one trial, 161 women; *very low-quality evidence*) (Brown 2017b).

Summary

Probably no difference between interventions: moderate-quality evidence.

- *Moderate-quality* evidence showed no clear difference for the breastfeeding at discharge for women with GDM who were treated with lifestyle intervention versus usual care or diet alone.

No conclusions possible: low to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence showed no clear difference for the breastfeeding at six weeks and six months or longer postpartum for women with GDM who were treated with lifestyle intervention versus usual care or diet alone.

20.0 Maternal mortality

Maternal mortality was reported as an outcome by one review (Brown 2017c) (Table 2.11; Table 2.19). The quality of the evidence was *very low- quality*.

Exercise versus control: There were no events of maternal mortality in either the exercise or the control group (RR not estimable; two trials, 48 women; *very low-quality evidence*) (Brown 2017c).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence showed no clear difference for the risk of maternal mortality for women with GDM who were treated with exercise versus control.

21.0 Sense of well-being and quality of life

Sense of well-being and quality of life of reported as an outcome by one review (Brown 2017b) (Table 2.11; Table 2.19). The outcome was reported during treatment and at three months postpartum using the Short Form Health Survey SF-36 (overall physical component, overall mental component and anxiety). The quality of the evidence ranged from *moderate- to low- quality.*

21.1 Sense of well-being and quality of life during treatment: Overall physical component

21.1.1 Lifestyle intervention versus usual care or diet alone: The evidence suggested an improvement for the overall physical component for sense of well-being and quality of life from the Short Form Health Survey (SF-36) during treatment for women with GDM in the lifestyle intervention group compared to usual care or diet alone group (MD 1.5, 95% CI 0.12 to 2.88; one trial, 682 women; *low-quality evidence*) (Brown 2017b).

21.2 Sense of well-being and quality of life during treatment: Overall mental component

21.2.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the overall mental component for sense of well-being and quality of life from the Short Form Health Survey (SF-36) during treatment for women with GDM between the lifestyle intervention and usual care or diet alone group (MD 1.30, 95% CI -0.17 to 2.77; one trial, 682 women; *low-quality evidence*) (Brown 2017b).

21.3 Sense of well-being and quality of life during treatment: Anxiety

21.3.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the anxiety component for sense of well-being and quality of life from the Short Form Health Survey (SF-36) during treatment for women with GDM between the lifestyle intervention and usual care or diet alone group (MD -0.30, 95% CI -0.88 to 0.28; one trial, 682 women; *moderate-quality evidence*) (Brown 2017b).

21.4 Sense of well-being and quality of life at three months post-partum: Overall physical component

21.4.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the overall physical component for sense of well-being and quality of life from the Short Form Health Survey (SF-36) at three months post-partum for women with GDM between the lifestyle intervention and usual care or diet alone group (MD 1.20, 95% CI -0.19 to 2.59; one trial, 573 women; *low quality evidence*) (Brown 2017b).

21.5 Sense of well-being and quality of life at three months post-partum: Overall mental component

21.5.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the overall mental component for sense of well-being and quality of life from the Short Form Health Survey (SF-36) at three months post-partum for women with GDM between the lifestyle intervention and usual care or diet alone group (MD 0.20, 95% CI -1.51 to 1.91; one trial, 573 women; *low-quality evidence*) (Brown 2017b).

21.6 Sense of well-being and quality of life at three months post-partum: Anxiety

21.6.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the anxiety component for sense of well-being and quality of life from the Short Form Health Survey (SF-36) at three months post-partum for women between the lifestyle intervention and usual care or diet alone group (MD -0.20, 95% CI -0.83 to 0.43; one trial, 573 women; *low-quality evidence*) (Brown 2017b).

Summary

Probably no difference between interventions: moderate-quality evidence

- *Moderate-quality* evidence showed no clear difference during treatment for the anxiety for sense of well-being and quality of life for women with GDM who were treated with lifestyle intervention versus usual care or diet alone.

No conclusions possible: low to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence of benefit suggested an improvement during treatment for the overall physical component and the overall mental component for sense of well-being and quality of life for women with GDM who were treated with lifestyle intervention compared to usual care or diet alone, but no clear difference at three months postpartum.

Summary

- *Low-quality* evidence showed no clear difference for anxiety at three months postpartum for women with GDM who were treated with lifestyle intervention compared to usual care or diet alone.

22.0 Women's view of the intervention

Women's views of the interventions were reported as an outcome by one review (Brown 2017c) (Table 2.11; Table 2.19). The quality of the evidence was *low-quality.*

22.1 Exercise versus control: The evidence suggested favourable views of the intervention for women with GDM, however the MD and SD were not estimable; one trial, 40 women; *low-quality evidence*) (Brown 2017c).

Summary

No conclusions possible: low to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested favourable views of the intervention for women with GDM treated with exercise compared with control.

23.0 Relevant biomarker changes associated with the intervention (including adiponectin, free fatty acids, triglycerides, high-density lipoproteins, low-density lipoproteins, insulin)

Relevant biomarker changes associated with the intervention were reported as an outcome by one review (Han 2017). The measures reported were Homeostasis Model Assessment Insulin Resistance (HOMA-IR), Quantitative Insulin Sensitivity Check Index (QUICKI) and fasting plasma insulin. The timing of the measures varied and included during treatment, at the end of treatment. three months postpartum and 38 weeks' gestation (Table 2.11; Table 2.19). The quality of the evidence ranged from *moderate- to very low- quality.*

23.1 Homeostasis Model Assessment Insulin Resistance (HOMA-IR) and HOMA2-IR

23.1.1 DASH diet versus control diet with matching macronutrient contents: The evidence suggested lower insulin resistance measured with HOMA-IR at the end of treatment for women with GDM in the DASH diet group compared to the control diet with matching macronutrient contents group (MD -1.00 %, 95% CI -1.34 to -0.66; one trial, 32 women; *moderate-quality evidence*) (Han 2017).

23.1.2 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for insulin sensitivity measured with HOMA2-IR at the end of treatment for women with GDM between the low-GI diet and high-fibre moderate-GI diet group (MD -0.10 %, 95% CI -0.38 to 0.18; one trial, 77 women; *very low-quality evidence*) (Han 2017).

23.1.3 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for insulin sensitivity measured with HOMA-IR at three months postpartum for women with GDM between the low-GI diet and high-fibre moderate-GI diet group (MD -0.30 %, 95% CI -0.66 to 0.06; one trial, 53 women; *very low-quality evidence*) (Han 2017).

23.1.4 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference for insulin sensitivity measured with HOMA-IR at the end of treatment for women with GDM between the diet recommendation + diet-related behavioural advice and diet recommendation only group (MD -0.30 %, 95% CI -0.77 to 0.17; one trial, 99 women; *very low-quality evidence*) (Han 2017).

23.1.5 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for insulin sensitivity measured with HOMA-IR at the end of the intervention for women with GDM in the soy protein-enriched diet and no soy protein diet group (MD -1.60 %, 95% CI -2.20 to 0.20; one trial, 68 women; *very low-quality evidence*) (Han 2017).

23.2 Quantitative Insulin Sensitivity Check Index (QUICKI)

23.2.1 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for insulin sensitivity measured with QUICKI at the end of the intervention for women with GDM in the soy protein-enriched diet and no soy protein diet group (MD 0.0, 95% CI -0.01 to 0.01; one trial, 68 women; *very low-quality evidence*) (Han 2017).

23.3 Fasting plasma insulin during the intervention

23.3.1 Energy restricted diet versus no energy restricted diet: There was no clear difference for insulin sensitivity (fasting plasma insulin) (during (gestation) not defined) for women with GDM between the energy restricted diet versus no energy restricted diet group (MD 100.00 pM, 95% CI -26.02 to 226.02; one trial, 12 women; *very low-quality evidence*) (Han 2017).

23.3.2 High unsaturated fat diet versus low unsaturated fat diet with matching calories: The evidence suggested higher fasting plasma insulin at 38 weeks' gestation for women with GDM in the high unsaturated fat diet group (MD 4.40 mU/L, 95% CI 2.59 to 6.21; one trial, 24 women; *very low-quality evidence*) (Han 2017).

23.3.3 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for insulin sensitivity measured in 10^{-5} min^{-1} per mU/L min at 38 weeks' gestation for women with GDM in the high unsaturated fat diet group (MD -0.08 mU/L min, 95% CI -0.21 to 0.05; one trial, 24 women; *very low-quality evidence*) (Han 2017).

23.4 Fasting plasma insulin at end of treatment

23.4.1 Energy restricted diet versus no energy restricted diet: There was no clear difference for fasting plasma insulin for women with GDM between the energy restricted diet and no energy restricted diet group (MD -20.00 pM, 95% CI -127.70 to 87.70; one trial, 12 women; *very low-quality evidence*) (Han 2017).

23.4.2 DASH diet versus control diet with matching macronutrient contents: The evidence suggested lower fasting plasma insulin for women with GDM in the DASH diet group compared to the control diet with matching macronutrient contents group (MD -3.26 µIU/mL, 95% CI -4.42 to -2.10; one trial, 32 women; *low-quality evidence*) (Han 2017).

23.4.3 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for insulin sensitivity - fasting plasma insulin for women with GDM between the low-GI diet and high-fibre moderate-GI diet group (MD 10.80 pmol/L, 95% CI -22.36 to 43.96; one trial, 70 women; *very low-quality evidence*) (Han 2017).

23.4.4 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference for fasting plasma insulin for women with GDM between the diet recommendation + diet-related behavioural advice and diet recommendation only group (MD -0.50 µIU/mL, 95% CI -2.69 to 1.69; one trial, 99 women; *very low-quality evidence*) (Han 2017).

23.4.5 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for fasting insulin for women with GDM in the soy protein-enriched diet and no soy protein diet group (MD -2.60 µIU/mL, 95% CI -8.03 to 2.83; one trial, 68 women; *very low-quality evidence*) (Han 2017).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence of benefit showed lower insulin resistance (measured with HOMA-IR) at the end of the intervention for women with GDM who were treated with the DASH diet compared to the control diet with matching macronutrient contents.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit by a reduced fasting plasma insulin for women with GDM who were treated with the DASH diet versus compared to a diet with matching macronutrient contents.
- *Very low-quality* evidence showed no clear difference for insulin resistance (measured with HOMA-IR or HOMA2-IR) for women with GDM who were treated with low-GI diet versus high-fibre moderate-GI diet; diet recommendation + diet-related behavioural advice versus diet recommendation only; soy protein-enriched diet versus no soy protein diet; or treated at three months postpartum with low-GI diet versus high-fibre moderate-GI diet. There was no evidence of a clear difference for insulin sensitivity for women with GDM who were treated with soy protein-enriched diet versus no soy protein diet (end with Quantitative Insulin Sensitivity Check Index (QUICKI); or high unsaturated fat diet versus low unsaturated fat diet with matching calories (during treatment; at 38 weeks' gestation). There was no clear evidence of a difference for fasting plasma insulin for women with GDM who were treated with energy restricted diet versus no energy restricted diet and no clear evidence of a difference for fasting plasma insulin at the end of the intervention for women with GDM who were treated with an energy restricted diet versus no energy restricted diet; low-GI diet versus high-fibre moderate-GI diet; diet recommendation + diet-related behavioural advice versus diet recommendation only; or soy protein-enriched diet versus no soy protein diet.
- *Very low-quality* evidence suggested harm by an increase for fasting plasma insulin (at 38 weeks' gestation) for women with GDM who were treated with high unsaturated fat diet group compared to low unsaturated fat diet with matching calories.

24.0 Pre-specified overview maternal secondary outcomes not reported in the included reviews

None of the included reviews reported data for behavioural changes associated with the treatment.

Secondary outcomes - Maternal long-term

25.0 Postnatal depression

Postnatal depression was reported as an outcome by one review (Brown 2017b) (Table 2.8; Table 2.19).

The quality of the evidence was *low-quality.*

25.1 Lifestyle intervention versus usual care or diet alone: The evidence suggested a decrease for the risk of developing postnatal depression (defined as Edinburgh Postnatal Depression Score (EPDS) >12) for women who had GDM in the lifestyle intervention group compared to the usual care or diet alone group (RR 0.49, 95% CI 0.31 to 0.78; one trial, 573 women; *low-quality evidence*) (Brown 2017b).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit by a decrease for the risk of developing postnatal depression for women with GDM who were treated with lifestyle intervention compared to usual care or diet alone.

26.0 Body Mass Index (BMI)

BMI was reported as an outcome by two reviews (Brown 2017b; Han 2017) (Table 2.12; Table 2.19). See Table 10. The timing of the assessment of BMI varied from three months (Han 2017) to 11 years (Brown 2017b). The quality of the evidence was *very low-quality.*

26.1 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference in BMI at three months postpartum for women who had GDM between the low-GI diet and high-fibre moderate-GI diet group (MD -0.50 kg/m^2, 95% CI -2.79 to 1.79; one trial, 52 women; *very low-quality evidence*) (Han 2017).

26.2 High unsaturated fat diet versus low unsaturated fat diet with matching calories: The evidence suggested a higher BMI at five to nine months postpartum for women who had GDM in the high unsaturated fat diet group compared to the low unsaturated fat diet with matching calories group (MD 4.10 kg/m^2, 95% CI 2.34 to 5.86; one trial, 27 women; *very low-quality evidence*) (Han 2017).

26.3 Lifestyle intervention versus usual care or diet alone: Evidence from two trials in the Brown (2017b) review showed no clear difference in BMI for women who had GDM between the lifestyle intervention and usual care or diet alone group (at 4.5 to 10 years follow-up in one trial (*moderate-quality evidence*) and 9 to 11 years follow-up in the other trial (*moderate-quality evidence*). The data in both trials were not in a format suitable for inclusion in a meta-analysis.

Summary

Probably no difference between interventions: Direction of effect suggested no difference.

- *Moderate-quality* evidence showed no clear difference for BMI at a maximum follow-up of 11 years for women with GDM who were treated with a lifestyle intervention versus usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

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Summary

- *Very low-quality* suggested evidence of harm by a higher BMI at five to nine months for women with GDM who were treated with high unsaturated fat diet compared to low unsaturated fat diet with matching calories.
- *Very low-quality* evidence showed no clear difference for BMI at three months for women with GDM who were treated with low-GI diet versus high-fibre moderate-GI diet.

27.0 Postnatal weight retention or return to pre-pregnancy weight

Postnatal weight retention or return to pre-pregnancy weight was reported as an outcome by three reviews (Brown 2017b; Brown 2017c; Han 2017) (Table 2.8; Table 2.19). The timing of the measurement of the outcome varied between reviews and was reported at six weeks, three months, seven months and twelve months. One review did not report the timing. The quality of the evidence ranged from *high- to very low-quality.*

27.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for return to pre-pregnancy weight (defined as the ability to meet postpartum weight goals at six weeks postpartum) for women who had GDM between the lifestyle intervention and usual care or diet alone group (RR 1.20, 95% CI 0.67 to 2.17; one trial, 189 women; *low-quality evidence*) (Brown 2017b).

27.2 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for return to pre-pregnancy weight (defined as returned to within one kg of their pre-pregnancy weight at three months postpartum) for women who had GDM between the low-GI diet and high-fibre moderate-GI diet group (RR 1.15, 95% CI 0.43 to 3.07; one trial, 55 women; *very low-quality evidence*) (Han 2017).

27.3 Lifestyle intervention versus usual care or diet alone: There was no clear difference for return to pre-pregnancy weight (defined as the ability to meet postpartum weight goals at seven months postpartum) for women who had GDM between the lifestyle intervention and usual care or diet alone group (RR 1.59, 95% CI 0.99 to 2.57; one trial, 159 women; *very low-quality evidence*) (Brown 2017b).

27.4 Lifestyle intervention versus usual care or diet alone: The evidence suggested that more women who had GDM met postpartum weight goals by returning to their pre-pregnancy weight (at twelve months postpartum) in the lifestyle intervention group compared to the usual care or diet alone group (RR 1.75, 95% CI 1.05 to 2.90; one trial, 156 women; *low-quality evidence*) (Brown 2017b).

27.5 Exercise versus control: There was no clear difference for return to pre-pregnancy BMI (at follow-up, timing not defined) for women who had GDM between the exercise and control group (MD 0.11 kg/m^2, 95% CI -1.04 to 1.26; three trials, 254 women; *high-quality evidence*) (Brown 2017c).

Summary

Effective interventions: high-quality evidence of effectiveness

- *High-quality* evidence showed no clear difference for the return to pre-pregnancy BMI (at follow-up, timing not defined) for women with GDM who were treated with exercise versus control.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested benefit by an increased number of women meeting postpartum weight goals, that is returning to their pre-pregnancy weight at twelve months postpartum for women with GDM who were treated with lifestyle intervention compared to usual care or diet alone.
- *Low-quality* evidence showed no clear difference for postnatal weight retention or return to pre-pregnancy weight at six weeks postpartum for women with GDM who were treated with lifestyle intervention versus usual care or diet alone.
- *Very low-quality* evidence showed no clear difference for postnatal weight retention or return to pre-pregnancy weight at three months postpartum for women with GDM who were treated with low-GI diet versus high-fibre moderate-GI diet; or lifestyle intervention versus usual care or diet alone at eight months postpartum.

28.0 Impaired glucose tolerance

Impaired glucose tolerance was reported as an outcome by two reviews (Brown 2017b; Han 2017) (Table 2.12; Table 2.19). The timing for the reporting of this outcome varied between reviews and included up to 2 weeks postpartum, three months postpartum, six months postpartum, four to 13 months postpartum and not defined. The measures used to determine impaired glucose tolerance also varied between reviews and included OGTT, fasting blood glucose and test was not defined. The quality of the evidence ranged from *low- to very low-quality.*

28.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of impaired glucose tolerance (test and timing not defined) for women who had GDM between the lifestyle intervention and usual care or diet alone group (RR 0.67, 95% CI 0.12 to 3.69; one trial, 56 women; *very low-quality evidence*) (Brown 2017b).

28.2 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for the risk of impaired glucose tolerance (defined as borderline OGTT at one to two

weeks postpartum) for women who had GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (RR 1.50, 95% CI 0.30 to 7.43; one trial, 24 women; *very low-quality evidence*) (Han 2017).

28.3 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for the risk of impaired glucose tolerance (measure not defined at three months postpartum) for women who had GDM between the low-GI diet and high-fibre moderate-GI diet group (RR 1.33, 95% CI 0.44 to 4.04; one trial, 58 women; *very low-quality evidence*) (Han 2017).

28.4 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of impaired glucose tolerance (fasting plasma glucose at three months postpartum) but a non-significant trend towards lower fasting glucose concentration for the women who had GDM in the lifestyle intervention group compared to the usual care or diet alone group (MD -0.08 mmol/L, 95% CI -0.16 to 0.00; one trial, 165 women; *low-quality evidence*) (Brown 2017b).

28.5 Lifestyle intervention versus usual care or diet alone: The evidence suggested fewer women had impaired glucose tolerance (defined as fasting blood glucose concentration at six months postpartum) for the women who had GDM in the lifestyle intervention group compared to the usual care or diet alone group (MD -0.14 mmol/L, 95% CI -0.22 to -0.06; one trial, 165 women; *low-quality evidence*) (Brown 2017b).

28.6 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for the risk of impaired glucose tolerance (defined as borderline OGTT at four to 13 months post-partum) for women who had GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (RR 0.27, 95% CI 0.01 to 4.93; one trial, 7 women; *very low-quality evidence*) (Han 2017).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit by a reduced impaired glucose tolerance at six months postpartum for women with GDM who were treated with lifestyle intervention compared to usual care or diet alone.
- *Low-quality* evidence showed no clear difference for the risk of impaired glucose tolerance for women with GDM who were treated with lifestyle intervention versus usual care or diet alone at three months postpartum.

Summary

- *Very low-quality* evidence showed no clear difference for the risk of impaired glucose tolerance for women with GDM who were treated with lifestyle intervention versus usual care or diet alone (timing not defined); high unsaturated fat diet versus low unsaturated fat diet with matching calories (at one to two weeks postpartum); low-GI diet versus high-fibre moderate-GI diet (at three months postpartum); or high unsaturated fat diet versus low unsaturated fat diet with matching calories (at 13 months postpartum.

29.0 Cardiovascular health (as defined in the reviews including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)

Cardiovascular health reported as metabolic syndrome was reported by one review (Brown 2017b) (Table 2.12; Table 2.19). The quality of the evidence was *low-quality.*

29.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of cardiovascular health at follow-up between 4.5 to 10 years after diagnosis of GDM for the women between the lifestyle intervention and usual care or diet alone group (RR 0.93, 95% CI 0.71 to 1.22; one trial, 430 women; *low-quality evidence*) (Brown 2017b).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the risk of metabolic syndrome for women with GDM who were treated lifestyle intervention versus usual care or diet alone.

30.0 Pre-specified overview maternal long-term secondary outcomes not reported in the included reviews

None of the included reviews reported data for the development of type 2 diabetes and subsequent gestational diabetes.

Secondary outcomes - Fetal/neonatal

31.0 Stillbirth

Stillbirth was reported as an outcome by four reviews (Brown 2017a; Brown 2017b; Brown 2017c; Han 2017) (Table 2.13; Table 2.19). There was no clear evidence of a difference for the risk of stillbirth for any of the comparisons reporting this outcome. The quality of the evidence ranged from *low- to very low-quality.*

31.1 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of stillbirth for babies born to mothers with GDM between the glibenclamide and placebo group (RR 0.49, 95% CI 0.05 to 5.38; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

31.2 Metformin versus glibenclamide: There was no clear difference for the risk of stillbirth for babies born to mothers with GDM between the metformin and glibenclamide group (RR 0.92, 95% CI 0.06 to 14.55; one trial, 200 babies; *very low-quality evidence*) (Brown 2017a).

31.3 Energy restricted diet versus no energy restricted diet: There was no clear difference for the risk of stillbirth for babies born to mothers with GDM between the energy restricted diet and no energy restricted diet group (RR not estimable; two trials, 423 babies; *low-quality evidence*) (Han 2017). There were no events of stillbirths reported in either group.

31.4 Low-carbohydrate diet versus high-carbohydrate diet: There was no clear difference for the risk of stillbirth for babies born to mothers with GDM between the low-carbohydrate and high-carbohydrate diet group (RR 3.00, 95% CI 0.12 to 72.49; one trial, 150 babies; *very low-quality evidence*) (Han 2017).

31.5 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of stillbirth for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.15, 95% CI 0.01 to 2.86; four trials, 2355 babies; *very low-quality evidence*) (Brown 2017b).

31.6 Exercise versus control: There were no events of stillbirth reported for babies born to mothers with GDM in either the exercise or the control groups (RR not estimable; one trial, 29 babies; *very low-quality evidence*) (Brown 2017c).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence reported no events for stillbirth for babies born to mothers with GDM who were treated with either energy restricted diet or no energy restricted diet.
- *Very low-quality* evidence showed no clear difference for the risk of stillbirth for babies born to mothers with GDM who were treated with glibenclamide versus placebo; metformin versus glibenclamide; low-carbohydrate diet versus high-carbohydrate diet; lifestyle intervention versus usual care or diet alone; or exercise versus control (no events).

32.0 Neonatal death

Neonatal death was reported as an outcome by three reviews (Brown 2017a; Brown 2017b; Han 2017) (Table 2.13; Table 2.19). There was no clear evidence of a difference for the risk of neonatal death for any of the comparisons reporting this outcome. The quality of the evidence ranged from *low- to very low-quality.*

32.1 Oral antidiabetic agents versus placebo: There were no events of neonatal death reported for babies born to mothers with GDM in either the glibenclamide or the placebo groups (RR not estimable; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

32.2 Energy restricted diet versus no energy restricted diet: There were no events of neonatal death reported for babies born to mothers with GDM in either the energy restricted diet or the no energy restricted diet groups (RR not estimable; two trials, 423 babies; *low-quality evidence*) (Han 2017).

32.3 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of neonatal death for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.73, 95% CI 0.22 to 2.42; five trials, 3055 babies; *low-quality evidence*) (Brown 2017b).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the risk of neonatal death for babies born to mothers with GDM who were treated with energy restricted diet versus no energy restricted diet (no events); or lifestyle intervention versus usual care or diet alone.
- *Very low-quality* evidence reported no events of neonatal death for babies born to mothers with GDM who were treated either with glibenclamide or placebo.

33.0 Macrosomia (> 4000 g; or as defined in the reviews)

Macrosomia was reported as an outcome by seven reviews (Boulvain 2001; Brown 2017a; Brown 2017b; Brown 2017c; Han 2012; Han 2017; Martis 2016a) (Table 2.13; Table 2.19). Definitions of macrosomia varied between reviews and included ≥ 3700 g; >4000 g; ≥ 4000 g; > 4500 g or not defined. The quality of the evidence ranged from *moderate- to very low-quality.*

33.1 Induction of labour versus expectant management: The evidence suggested a reduction for the risk of macrosomia (> 4000 g) for babies born to mothers with GDM in the induction of labour group

compared to the expectant management group (RR 0.56, 95% CI 0.32 to 0.98; one trial, 200 babies; *very low-quality evidence*) (Boulvain 2001).

33.2 Oral antidiabetic agents versus placebo: There was no difference for the risk of macrosomia (≥ 4000 g) for babies born to mothers with GDM between the glibenclamide and placebo group (RR 0.71, 95% CI 0.36 to 1.41; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

33.3 Metformin versus glibenclamide: There was no clear difference for the risk of macrosomia (≥ 4000 g in one trial and ≥ 3700 g in one trial) for babies born to mothers with GDM between the metformin and glibenclamide group (RR 0.72, 95% CI 0.23 to 2.21; two trials, 308 babies; *low-quality evidence*) (Brown 2017a).

33.4 Glibenclamide versus acarbose: There was no clear difference for the risk of macrosomia (> 4000 g) for babies born to mothers with GDM between the glibenclamide and acarbose group (RR 7.20, 95% CI 0.41 to 125.97; one trial, 43 babies; *very low-quality evidence*) (Brown 2017a).

33.5 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the risk of macrosomia (> 4000 g) for babies born to mothers with GDM between the low-moderate GI diet and moderate-high GI diet group (RR 0.59, 95% CI 0.16 to 2.26; three trials, 172 babies; *very low-quality evidence*) (Han 2017).

33.6 Energy restricted diet versus no energy restricted diet: There was no clear difference for the risk of macrosomia (> 4000 g) for babies born to mothers with GDM between the energy restricted diet and no energy restricted diet group (RR 0.99, 95% CI 0.64 to 1.53; two trials, 421 babies; *very low-quality evidence*) (Han 2017).

33.7 Energy restricted diet versus no energy restricted diet: There was no clear difference for the risk of macrosomia (> 4500 g) for babies born to mothers with GDM between the energy restricted diet and no energy restricted diet group (RR 1.01, 95% CI 0.33 to 3.05; one trial, 299 babies; *very low-quality evidence*) (Han 2017).

33.8 DASH diet versus control diet with matching macronutrient contents: The evidence suggested a reduced risk of macrosomia (≥ 4000 g) for babies born to mothers with GDM in the DASH diet group compared to the control diet with matching macronutrient contents (RR 0.10, 95% CI 0.01 to 0.73; one trial, 52 babies; *very low-quality evidence*) (Han 2017).

33.9 Low-carbohydrate diet versus high-carbohydrate diet: There was no clear difference for the risk of macrosomia (> 4000 g) for babies born to mothers with GDM between the low-carbohydrate and high-carbohydrate diet group (RR 0.20, 95% CI 0.02 to 1.69; two trials, 179 babies; *low-quality evidence*) (Han 2017).

33.10 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for the risk of macrosomia (> 4000 g) for babies born to mothers with GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (RR 0.53, 95% CI 0.18 to 1.56; two trials, 111 babies; *low-quality evidence*) (Han 2017).

33.11 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for the risk of macrosomia (> 4000 g) for babies born to mothers with GDM between the low-GI diet and high-fibre moderate-GI diet group (RR 0.32, 95% CI 0.03 to 2.96; one trial, 92 babies; *very low-quality evidence*) (Han 2017).

33.12 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for the risk of macrosomia (> 4000 g) for babies born to mothers with GDM between the soy protein-enriched diet and no soy protein diet group (RR 0.60, 95% CI 0.16 to 2.31; one trial, 68 babies; *very low-quality evidence*) (Han 2017).

33.13 Ethnic specific diet versus standard healthy diet: There was no clear difference for the risk of macrosomia (> 4000 g) for babies born to mothers with GDM between the ethnic specific diet and standard healthy diet group (RR 0.20 g, 95% CI 0.01 to 3.70; one trial, 20 women; *very low-quality evidence*) (Han 2017).

33.14 Lifestyle intervention versus usual care or diet alone: The evidence suggested a reduced risk of macrosomia (> 4 kg in five trials and ≥ 4 kg in two trials) for babies born to mothers with GDM in the lifestyle intervention group compared to the usual care or diet alone (average RR 0.64, 95% CI 0.48 to 0.87; seven trials, 3422 babies; *low-quality evidence*) (Brown 2017b).

33.15 Exercise versus control: There was no clear difference for the risk of macrosomia (not defined in the review) for babies born to mothers with GDM between the exercise and control group (RR 0.69, 95% CI 0.35 to 1.35; five trials, 296 babies; *moderate-quality evidence*) (Brown 2017c).

33.16 Intensive management versus routine care: The evidence suggested a reduced risk of macrosomia (≥ 4000 g) for babies born to mothers with GDM in the intensive management group compared to the routine care group (RR 0.38, 95% CI 0.19 to 0.74; three trials, 438 babies; *moderate-quality evidence*) (Han 2012).

33.17 Strict intensity of glycaemic control versus less strict glycaemic control: There was no clear difference for the risk of macrosomia (> 4000 g) for babies born to mothers with GDM between the strict intensity of glycaemic control and less strict glycaemic control group (RR 1.35, 95% CI 0.31 to 5.85; one trial, 171 babies; *very low-quality evidence*) (Martis 2016a).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence suggested a benefit by a reduction for the risk of macrosomia (≥ 4000 g) for babies born to mothers with GDM who were treated with intensive management compared to routine care.
- *Moderate-quality* evidence showed no clear difference for the risk of macrosomia (not defined) for babies born to mothers with GDM who were treated with exercise versus control.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit by a reduced risk of macrosomia for babies born to mothers with GDM who were treated with lifestyle intervention compared to usual care or diet alone (> 4 kg (5 trials) (≥ 4 kg (2 trials).
- *Very low-quality* evidence suggested a benefit by a reduced risk of macrosomia for babies born to mothers with GDM who were treated with induction of labour compared to expectant management (> 4000 g); or the DASH diet compared to control diet with matching macronutrient contents (≥ 4000 g).
- *Low-quality* evidence showed no clear difference for the risk of macrosomia for babies born to mothers with GDM who were treated with metformin versus glibenclamide (≥ 4000 g (1 trial) (≥ 3700 g (1 trial); low-carbohydrate diet versus high-carbohydrate diet (> 4000 g); or high unsaturated fat diet versus low unsaturated fat diet with matching calories (> 4000 g).
- *Very low-quality* evidence showed no clear difference for the risk of macrosomia for babies born to mothers with GDM who were treated with glibenclamide versus placebo (≥ 4000 g); glibenclamide versus acarbose (> 4000 g); low-moderate GI diet versus moderate-high GI diet (> 4000 g); energy restricted diet versus no energy restricted diet (> 4000 g and 4500 g); low-GI diet versus high-fibre moderate-GI diet (> 4000 g); soy protein-enriched diet versus no soy protein diet (> 4000 g); ethnic specific diet versus standard healthy diet (> 4000 g); or strict intensity of glycaemic control versus less strict glycaemic control (> 4000 g).

34.0 Small-for-gestational age (SGA)

SGA was reported as an outcome by five reviews (Brown 2017a; Brown 2017b; Han 2012; Han 2017; Martis 2016a) (Table 2.13; Table 2.19). No definition of SGA was reported in the reviews. There was no

clear evidence of a difference for the risk of being born SGA for any of the comparisons reporting this outcome. The quality of the evidence ranged from *moderate-to very low-quality.*

34.1 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of SGA for babies born to mothers with GDM between the glibenclamide and placebo group (RR 1.11, 95% CI 0.58 to 2.10; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

34.2 Glibenclamide versus acarbose: There were no events of SGA for babies born to mothers with GDM in either the glibenclamide or the acarbose group (RR not estimable; one trial, 43 babies; *low-quality evidence*). There were no events of SGA reported in either groups (Brown 2017a).

34.3 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the risk of SGA for babies born to mothers with GDM between the low-moderate GI diet and moderate-high GI diet group (RR 5.16, 95% CI 0.26 to 103.27; one trial, 63 babies; *very low-quality evidence*) (Han 2017).

34.4 Low-carbohydrate diet versus high-carbohydrate diet: There was no clear difference for the risk of SGA for babies born to mothers with GDM between the low-carbohydrate and high-carbohydrate diet group (RR 0.68, 95% CI 0.29 to 1.56; one trial, 149 babies; *low-quality evidence*) (Han 2017).

34.5 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for the risk of SGA for babies born to mothers with GDM between the low-GI diet and high-fibre moderate-GI diet group (RR 1.20, 95% CI 0.34 to 4.18; one trial, 92 babies; *very low-quality evidence*) (Han 2017).

34.6 Ethnic specific diet versus standard healthy diet: There was no clear difference for the risk of SGA for babies born to mothers with GDM between the ethnic specific diet and standard healthy diet group (RR 0.33, 95% CI 0.02 to 7.32; one trial, 20 babies; *very low-quality evidence*) (Han 2017).

34.7 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of SGA for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.98, 95% CI 0.73 to 1.32; four trials, 2324 babies; *moderate-quality evidence*) (Brown 2017b).

34.8 Intensive management versus routine care: There was no clear difference for the risk of SGA for babies born to mothers with GDM between the intensive management and routine care group (RR 1.53, 95% CI 0.81 to 2.88; three trials, 509 babies; *very low-quality evidence*) (Han 2012).

34.9 Strict intensity of glycaemic control versus less strict glycaemic control: There was no clear difference for the risk of SGA for babies born to mothers with GDM between the strict intensity of glycaemic control and less strict glycaemic control group (RR 1.12, 95% CI 0.48 to 2.63; one trial, 171 babies; *very low-quality evidence*) (Martis 2016a).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed no clear difference for the risk of SGA for babies born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the risk of SGA for babies born to mothers with GDM who were treated with glibenclamide versus acarbose (no events); or low-carbohydrate diet versus high-carbohydrate diet.

- *Very low-quality* evidence showed no clear difference for the risk of SGA for babies born to mothers with GDM who were treated with glibenclamide versus placebo; low-moderate GI diet versus moderate-high GI diet; ethnic specific diet versus standard healthy diet; low-GI diet versus high-fibre moderate-GI diet; intensive management versus routine care; or strict intensity of glycaemic control versus less strict glycaemic control.

35.0 Birth trauma (e.g. shoulder dystocia, bone fracture, nerve palsy)

Birth trauma was reported as an outcome by five reviews (Boulvain 2001; Brown 2017a; Brown 2017b; Han 2012; Han 2017) (Table 2.13; Table 2.19). Birth trauma was variously shoulder dystocia, bone fracture, nerve palsy or as a general term of birth trauma that was not further defined. The quality of the evidence ranged from *low- to very low-quality.*

35.1 Birth trauma (not defined)

35.1.1 Metformin versus glibenclamide: There were no events of birth trauma for babies born to mothers with GDM in either the metformin or the glibenclamide group (RR not estimable; one trial, 159 babies; *low-quality evidence*) (Brown 2017a).

35.1.2 Glibenclamide versus acarbose: There were no events of birth trauma for babies born to mothers with GDM in either the glibenclamide or the acarbose group (RR not estimable; one trial, 43 babies; *low-quality evidence*) (Brown 2017a).

35.1.3 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of birth trauma for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.48, 95% CI 0.12 to 1.90; three trials, 1930 babies; *low-quality evidence*) (Brown 2017b).

35.2 Birth trauma: Shoulder dystocia

35.2.1 Induction of labour versus expectant management: The evidence suggested a reduction in the risk of shoulder dystocia for babies of mothers with GDM whose labour was induced at 38 completed weeks of gestation compared to the expectant management group (RR 0.14, 95% CI 0.01 to 2.73; one trial, 200 babies; *very low-quality evidence*). There were three babies with shoulder dystocia in the expectant management group (Boulvain 2001).

35.2.2 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of shoulder dystocia for babies born to mothers with GDM between the glibenclamide and placebo group (RR 0.33, 95% CI 0.01 to 8.00; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

35.2.3 Metformin versus glibenclamide: There was no clear difference for the risk of shoulder dystocia for babies born to mothers with GDM between the metformin and glibenclamide group (RR 0.99, 95% CI 0.14 to 6.89; two trials, 195 babies; *low-quality evidence*) (Brown 2017a).

35.2.4 Energy restricted diet versus no energy restricted diet: There was no clear difference for the risk of shoulder dystocia for babies born to mothers with GDM between the energy restricted diet and no energy restricted diet group (RR 0.12, 95% CI 0.01 to 2.26; two trials, 418 babies; *very low-quality evidence*) (Han 2017).

35.2.5 Intensive management versus routine care: There was no clear difference for the risk of shoulder dystocia for babies born to mothers with GDM between the intensive management and routine care group (RR 0.69, 95% CI 0.06 to 7.27; one trial, 83 babies; *very low-quality evidence*) (Han 2012).

35.2.6 Lifestyle intervention versus usual care or diet alone: The evidence suggested a reduction in the risk of shoulder dystocia for babies born to mothers with GDM in the lifestyle intervention group compared to the usual care or diet alone group (RR 0.38, 95% CI 0.21 to 0.66; five trials, 2894 babies; *low-quality evidence*) (Brown 2017b).

35.3 Birth trauma: Bone fracture

35.3.1 Induction of labour versus expectant management: There were no events of bone fracture for babies born to mothers with GDM in either the induction of labour or the expectant management group (RR not estimable; one trial, 200 babies; *very low-quality evidence*). There were no events of bone fracture reported in either group (Boulvain 2001).

35.3.2 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of bone fracture for babies born to mothers with GDM between the glibenclamide and placebo group (RR 0.74, 95% CI 0.17 to 3.25; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

35.3.3. Energy restricted diet versus no energy restricted diet: There were no events of risk of bone fracture for babies born to mothers with GDM in either the energy restricted diet or the no energy restricted diet group (RR not estimable; one trial, 299 babies; *low-quality evidence*) (Han 2012).

35.3.4 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of bone fracture for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.35, 95% CI 0.01 to 8.45; two trials, 1730 babies; *low-quality evidence*). Event rates were very low with one being reported in the control group (Brown 2017b).

35.4 Birth trauma: Nerve palsy (brachial plexus)

35.4.1 Induction of labour versus expectant management: There were no events of nerve palsy for babies born to mothers with GDM in either the induction of labour or the expectant management group (RR not estimable; one trial, 200 babies; *very low-quality evidence*) (Boulvain 2001).

35.4.2 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of nerve palsy for babies born to mothers with GDM between the glibenclamide and placebo group (RR 0.33, 95% CI 0.01 to 8.00; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

35.4.3 Energy restricted diet versus no energy restricted diet: There were no events of nerve palsy for babies born to mothers with GDM between the energy restricted diet versus no energy restricted diet group (RR not estimable; one trial, 299 babies; *low-quality evidence*) (Han 2017).

35.4. 4 Lifestyle interventions versus usual care or diet alone: There was no clear difference for the risk of nerve palsy for babies born to mothers with GDM between the lifestyle intervention and usual

care or diet alone group (RR 0.15, 95% CI 0.01 to 2.86; one trial, 1030 babies; *low-quality evidence*). Event rates were very low with three being reported in the control group (Brown 2017b).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit for a reduced risk of shoulder dystocia for babies born to mothers with GDM who were treated with lifestyle intervention compared to usual care or diet alone.
- *Very low-quality* evidence suggested a benefit for a reduced risk of shoulder dystocia for babies born to mothers with GDM who were treated with induction of labour compared to expectant management.
- *Low-quality* evidence showed no clear difference for the risk of birth trauma for babies born to mothers with GDM who were treated with metformin versus glibenclamide (not defined, no events); glibenclamide versus acarbose (not defined, no events); lifestyle intervention versus usual care or diet alone (not defined); metformin versus glibenclamide (shoulder dystocia); energy restricted diet versus no energy restricted diet (bone fracture and nerve palsy, no events); lifestyle intervention versus usual care or diet alone (bone fracture); or lifestyle intervention versus usual care or diet alone (nerve palsy).
- *Very low-quality* evidence showed no clear difference for the risk of birth trauma for babies born to mothers with GDM who were treated with glibenclamide versus placebo (shoulder dystocia); energy restricted diet versus no energy restricted diet (shoulder dystocia); intensive management versus routine care (shoulder dystocia); induction of labour versus expectant management (bone fracture); glibenclamide versus placebo (bone fracture); induction of labour versus expectant management (bone fracture and nerve palsy, no events); or glibenclamide versus placebo (nerve palsy).

36.0 Gestational age at birth

Gestational age at birth was reported as an outcome by seven reviews (Brown 2016a; Brown 2017a; Brown 2017b; Brown 2017c; Han 2012; Han 2017; Martis 2016a) (Table 2.13; Table 2.19). The quality of the evidence ranged from *moderate- to very low-quality.*

36.1 Oral antidiabetic agents versus placebo: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the oral antidiabetic drug glibenclamide and placebo group (MD 0.0 weeks, 95% CI -0.32 to 0.32; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

36.2 Metformin versus glibenclamide: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the metformin and glibenclamide group (MD 0.03 weeks, 95% CI -0.22 to 0.28; three trials, 508 babies; *very low-quality evidence*) (Brown 2017a).

36.3 Glibenclamide versus acarbose: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the glibenclamide and acarbose group (MD -0.10 weeks, 95% CI -0.82 to 0.62; one trial, 43 babies; *low-quality evidence*) (Brown 2017a).

36.4 Myo-inositol versus placebo: Myo-inositol was associated with being born at a later gestational age for babies of mothers compared with placebo (MD 2.1 weeks, 95% CI 1.27 to 2.93; one trial, 73 babies; *moderate-quality evidence*) (Brown 2016a).

36.5 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the low-moderate GI diet and moderate-high GI diet group (MD 0.30 weeks, 95% CI -0.30 to 0.90; one trial, 62 babies; *very low-quality evidence*) (Han 2017).

36.6 Energy restricted diet versus no energy restricted diet: There was no clear difference for gestational age at birth for babies born to mothers between the energy restricted diet and no energy restricted diet group (MD -0.16 weeks, 95% CI -0.67 to 0.36; two trials, 423 babies; *moderate-quality evidence*) (Han 2017).

36.7 DASH diet versus control diet with matching macronutrient contents: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the DASH diet and control diet with matching macronutrient contents group (MD 0.20 weeks, 95% CI -0.45 to 0.85; one trial, 52 babies; *very low-quality evidence*) (Han 2017).

36.8 Low-carbohydrate diet versus high-carbohydrate diet: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the low-carbohydrate and high-carbohydrate diet group (MD 0.10 weeks, 95% CI -0.42 to 0.62; two trials, 180 babies; *low-quality evidence*) (Han 2017).

36.9 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (MD 0.25 weeks, 95% CI -0.51 to 1.01; two trials, 111 babies; *low-quality evidence*) (Han 2017).

36.10 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the low-GI diet and high-fibre moderate-GI

diet group (MD -0.10 weeks, 95% CI -0.39 to 0.19; one trial, 92 babies; *low-quality evidence*) (Han 2017).

36.11 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the soy protein-enriched diet and no soy protein diet group (MD 0.40 weeks, 95% CI -0.23 to 1.03; one trial, 68 babies; *very low-quality evidence*) (Han 2017).

36.12 High-fibre diet versus standard-fibre diet: There was no clear difference for gestational age at birth for babies born to mothers with GDM between high-fibre diet and standard-fibre diet (MD 0.0 weeks, 95% CI -1.30 to 1.30; one trial, 22 babies; *very low-quality evidence*) (Han 2017).

36.13 Ethnic specific diet versus standard healthy diet: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the ethnic specific diet and standard healthy diet group (MD -0.40 weeks, 95% CI -1.15 to 0.35; one trial, 20 babies; *very low-quality evidence*) (Han 2017).

36.14 Lifestyle intervention versus usual care or diet alone: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (MD 0.04 weeks, 95% CI -0.13 to 0.20; five trials, 2057 babies; *low-quality evidence*) (Brown 2017b).

36.15 Exercise versus control: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the exercise and control group (MD-0.01 weeks, 95% CI -0.40 to 0.38; four trials, 167 babies; *low-quality evidence*) (Brown 2017c).

36.16 Intensive management versus routine care: There was no clear difference for gestational age at birth for babies born to mothers with GDM between the intensive management and routine care group (MD -0.18 weeks, 95% CI -0.43 to 0.07; four trials, 521 babies; *very low-quality evidence*) (Han 2012).

36.17 Strict intensity of glycaemic control versus less strict glycaemic control: There was no clear difference for gestational age at birth for babies to mothers with GDM between the strict intensity of glycaemic control and less strict glycaemic control group (MD -0.30 weeks, 95% CI -0.73 to 0.13; one trial, 171 babies; *very low-quality evidence*) (Martis 2016a).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence suggested a benefit for birth at a later gestational age for babies of mothers with GDM who were treated with myo-inositol compared to placebo.

Probably no difference between interventions: moderate-quality evidence; direction of the effect suggests benefit, but more evidence needed.

- *Moderate-quality* evidence showed no clear difference for the risk of low gestational age at birth for babies born to mothers with GDM who were treated with energy restricted diet versus no energy restricted diet.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed.

- *Low-quality* evidence showed no clear difference for the risk of low gestational age at birth for babies born to mothers with GDM who were treated with glibenclamide versus acarbose; low-carbohydrate diet versus high-carbohydrate diet; high unsaturated fat diet versus low unsaturated fat diet with matching calories; low-GI diet versus high-fibre moderate-GI diet; soy protein-enriched diet versus no soy protein diet; lifestyle intervention versus usual care; or diet alone or exercise versus control.
- *Very low-quality* evidence showed no clear difference for the risk of low gestational age at birth for babies born to mothers with GDM who were treated with glibenclamide versus placebo; metformin versus glibenclamide; DASH diet versus control diet with matching macronutrient contents; low-moderate GI diet versus moderate-high GI diet; high-fibre diet versus standard-fibre diet; ethnic specific diet versus standard healthy diet; intensive management versus routine care; or strict intensity of glycaemic control versus less strict glycaemic control.

37.0 Preterm birth (< 37 weeks' gestation and < 32 weeks' gestation)

Preterm birth was reported as an outcome by six reviews (Brown 2016a; Brown 2017b; Brown 2017c; Brown 2017a; Han 2012; Han 2017) (Table 2.13; Table 2.19).

None of the reviews reported data for preterm birth <32 weeks' gestation. The quality of the evidence ranged from *moderate- to very low-quality.*

37.1 Metformin versus glibenclamide: There was no clear difference for the risk of preterm birth (< 37 weeks) for babies born to mothers with GDM between the metformin and glibenclamide group (RR 1.59, 95% CI 0.59 to 4.29; three trials, 508 babies; *very low-quality evidence*) (Brown 2017a).

37.2 Glibenclamide versus acarbose: There were no events of preterm birth (< 37 weeks) for babies born to mothers with GDM in either the glibenclamide or the acarbose group (RR not estimable; one trial, 43 babies; *low-quality evidence*) (Brown 2017a).

37.3 Myo-inositol versus placebo: There was no clear difference for the risk of preterm birth (< 37 weeks) for babies born to mothers with GDM between in the myo-inositol and the placebo group (RR 1.00, 95% CI 0.09 to 10.56; one trial, 84 babies; *very low-quality evidence*) (Brown 2016a).

37.4 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the risk of preterm birth (< 37 weeks) for babies born to mothers with GDM between the low-moderate GI diet and moderate-high GI diet group (RR 0.64, 95% CI 0.22 to 1.85; two trials, 146 babies; *low-quality evidence*) (Han 2017).

37.5 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There were no events of preterm birth (< 37 weeks) for babies born to mothers with GDM in either the high unsaturated fat diet or the low unsaturated fat diet with matching calories group (RR not estimable; one trial, 84 babies; *low-quality evidence*) (Han 2017).

37.6 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for the risk of preterm birth (< 37 weeks) for babies born to mothers between the low-GI diet and high-fibre moderate-GI diet group (RR 0.96, 95% CI 0.14 to 6.53; one trial, 96 babies; *very low-quality evidence*) (Han 2017).

37.7 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference for the risk of preterm birth (< 37 weeks) for babies born to mothers with GDM between the diet recommendation + diet-related behavioural advice and diet recommendation only group (RR 0.51, 95% CI 0.10 to 2.66; one trial, 99 babies; *very low-quality evidence*) (Han 2017).

37.8 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for the risk of preterm birth (defined as < 37 weeks gestation in the review) for babies born to mothers with GDM between the soy protein-enriched diet and no soy protein diet group (RR 2.00, 95% CI 0.19 to 21.03; one trial, 68 babies; *very low-quality evidence*) (Han 2017).

37.9 Lifestyle intervention versus usual care or diet alone: The evidence suggested a reduced risk of preterm birth (< 37 weeks) for babies born to mothers with GDM in the lifestyle intervention group compared to the usual care or diet alone group (RR 0.71, 95% CI 0.53 to 0.96; three trials, 1797 babies; *moderate-quality evidence*) (Brown 2017b).

37.10 Exercise versus control: There was no clear difference for the risk of preterm birth (not defined) for babies born to mothers with GDM between the exercise and control group (RR 0.95, 95% CI 0.39 to 2.36; five trials, 302 babies; *low-quality evidence*) (Brown 2017c).

37.11 Intensive management versus routine care: There was no clear difference for the risk of preterm birth (< 37 weeks) for babies born to mothers with GDM between the intensive management and routine care group (RR 1.00, 95% CI 0.26 to 3.82; two trials, 138 babies; *low-quality evidence*) (Han 2012).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence of benefit showed a reduction for the risk of preterm birth for babies born to mothers with GDM who were treated with lifestyle intervention compared to usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the risk of preterm birth for babies born to mothers with GDM who were treated with glibenclamide versus acarbose (no events); low-moderate GI diet versus moderate-high GI diet; high unsaturated fat diet versus low unsaturated fat diet with matching calories (no events); exercise versus control (not defined); or intensive management versus routine care.
- *Very low-quality* evidence showed no clear difference for the risk of preterm birth for babies born to mothers with GDM who were treated with metformin versus glibenclamide; myo-inositol versus placebo; low-GI diet versus high-fibre moderate-GI diet; diet recommendation + diet-related behavioural advice versus diet recommendation only; or soy protein-enriched diet versus no soy protein diet.

38.0 Five-minute Apgar < 7

A five-minute Apgar score <7 was reported as an outcome by three reviews (Brown 2017a; Brown 2017b; Brown 2017c) (Table 2.13; Table 2.29). There was no clear evidence of a difference for the risk five-minute Apgar <7 for any of the comparisons reporting this outcome. The quality of the evidence ranged from *moderate- to very low-quality.*

38.1 Metformin versus glibenclamide: There were no events of a five-minute Apgar < 7 score for babies born to mothers with GDM in either the metformin or the glibenclamide group (RR not estimable; one trial, 149 babies; *low-quality evidence*) (Brown 2017a).

38.2 Lifestyle intervention versus usual care or diet alone: There was no clear difference for of a five-minute Apgar < 7 score for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.56, 95% CI 0.21 to 1.52; one trial, 1030 babies; *moderate-quality evidence*) (Brown 2017b).

38.3 Exercise versus control: There was no clear difference for of a five-minute Apgar < 7 score for babies born to mothers with GDM between the exercise and control group (RR 0.33, 95% CI 0.01 to 7.65; one trial, 34 babies; *very low-quality evidence*) (Brown 2017c).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed no clear difference for the risk of five-minute Apgar < 7 at birth for babies born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the risk of five-minute Apgar < 7 at birth for babies born to mothers with GDM who were treated with metformin versus glibenclamide.
- *Very low-quality* evidence showed no clear difference for the risk of five-minute Apgar < 7 at birth for babies born to mothers with GDM who were treated with exercise versus control.

39.0 Birthweight and z score

Birthweight was reported as an outcome by seven reviews (Brown 2016a; Brown 2017a; Brown 2017b; Brown 2017c; Han 2012; Han 2017; Martis 2016a) Table 2.13; Table 2.19). None of the included reviews reported data for birthweight z scores. The quality of the evidence ranged from *moderate- to very low-quality.*

39.1 Oral antidiabetic agents versus placebo: There was no clear difference in birthweight for babies born to mothers with GDM between the glibenclamide and placebo group (MD -33.0 g, 95% CI -134.53 to 68.53; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

39.2 Metformin versus glibenclamide: The evidence suggested a reduced birthweight for babies born to mothers with GDM in the metformin group compared to the glibenclamide group (MD -209.13 g, 95% CI -314.53 to 103.73; two trials, 349 babies; *very low-quality evidence*) (Brown 2017a).

39.3 Glibenclamide versus acarbose: There was no clear difference in birthweight for babies born to mothers with GDM between the glibenclamide and acarbose group (MD 153.0 g, 95% CI -123.52 to 429.52; one trial, 43 babies; *very low-quality evidence*) (Brown 2017a).

39.4 Myo-inositol versus placebo: There was no clear difference in birthweight for babies born to mothers with GDM between in the myo-inositol group and the placebo group (MD 16.00 g, 95% CI -209.72 to 241.72; one trial, 73 babies; *low-quality evidence*) (Brown 2016a).

39.5 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference in birthweight for babies born to mothers with GDM between the low-moderate GI diet and moderate-high GI diet group (MD -55.98 g, 95% CI -201.90 to 89.95; two trials, 145 babies; *very low-quality evidence*) (Han 2017).

39.6 Energy restricted diet versus no energy restricted diet: There was no clear difference in birthweight for babies born to mothers with GDM between the energy restricted diet and no energy restricted diet group (MD -107.00 g, 95% CI -240.32 to 26.32; one trial, 299 babies; *very low-quality evidence*) (Han 2017).

39.7 DASH diet versus control diet with matching macronutrient contents: The evidence suggested a reduced birthweight for babies born to mothers with GDM in the DASH diet group compared to the control diet with matching macronutrient contents (MD -.581.27 g, 95% CI -790.32 to -372.22; two trials, 86 babies; *moderate-quality evidence*) (Han 2017).

39.8 Low-carbohydrate diet versus high-carbohydrate diet: There was no clear difference in birthweight for babies born to mothers with GDM between the low-carbohydrate and high-carbohydrate diet group (MD 22.00 g, 95% CI -241.06 to 285.06; one trial, 30 babies; *very low-quality evidence*) (Han 2017).

39.9 High unsaturated fat diet versus low unsaturated fat diet with matching calories: There was no clear difference for birthweight for babies born to mothers between the high unsaturated fat diet and low unsaturated fat diet with matching calories group (MD -138.19 g, 95% CI -292.59 to 16.21; two trials, 111 babies; *low-quality evidence*) (Han 2017)

39.10 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for birthweight for babies born to mothers with GDM between the low-GI diet and high-fibre moderate-GI diet group (MD 0.0 g, 95% CI -277.18 to 277.18; one trial, 92 babies; *very low-quality evidence*) (Han 2017).

39.11 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for birthweight for babies born to mothers with GDM between the soy protein-enriched diet and no soy protein diet group (MD -142.60 g, 95% CI -360.40 to 75.20; one trial, 68 babies; *very low-quality evidence*) (Han 2017).

39.12 High-fibre diet versus standard-fibre diet: There was no clear difference for birthweight for babies born to mothers with GDM between high-fibre diet and standard-fibre diet (MD -94.00 g, 95% CI -446.71 to 258.71; one trial, 22 babies; *very low-quality evidence*) (Han 2017).

39.13 Ethnic specific diet versus standard healthy diet: There was no clear difference for birthweight for babies born to mothers with GDM between the ethnic specific diet and standard healthy diet group (MD -370.00 g, 95% CI -928.87 to 188.87; one trial, 20 babies; *very low-quality evidence*) (Han 2017).

39.14 Lifestyle intervention versus usual care or diet alone: The evidence suggested a reduced birthweight for babies born to mothers with GDM in the lifestyle intervention group compared to the usual care or diet alone group (MD -109.64 g, 95% CI -149.77 to -69.51; six trials, 3074 babies, *moderate-quality evidence*) (Brown 2017b). This was without a consequent increase in the risk of SGA as previously reported.

39.15 Exercise versus control: There was no clear difference for birthweight for babies born to mothers with GDM between the exercise and control group (MD -61.50 g, 95% CI -195.21 to 72.20; six trials, 192 babies; *very low-quality evidence*) (Brown 2017c).

39.16 Intensive management versus routine care: The evidence suggested a reduced birthweight for babies born to mothers with GDM in the intensive management compared to the routine care group (MD -117.33 g, 95% CI -198.72 to -35.94; four trials, 521 babies; *very low-quality evidence*) (Han 2012).

39.17 Strict intensity of glycaemic control versus less strict glycaemic control: There was no clear difference for birthweight for babies born to mothers with GDM between the strict intensity of glycaemic control and less strict glycaemic control group ((MD -0.92 g, 95% CI -241.97 to 57.97; one trial, 171 babies; *very low-quality evidence*) (Martis 2016a).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence of benefit showed a reduction of birthweight for babies born to mothers with GDM who were treated with the DASH diet compared to the control diet with matching macronutrient contents; or women with GDM treated with a lifestyle intervention compared to usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence of benefit showed a reduction of birthweight for babies born to mothers with GDM who were treated with metformin compared to glibenclamide, with no clear difference to gestational age at birth, SGA not reported.
- *Low-quality* evidence showed no clear difference for birthweight for babies born to mothers with GDM who were treated with myo-inositol versus placebo; or high unsaturated fat diet versus low unsaturated fat diet with matching calories.
- *Very low-quality* evidence showed no clear difference for the birthweight for babies born to mothers with GDM who were treated with glibenclamide versus placebo; glibenclamide versus acarbose; low-moderate GI diet versus moderate-high GI diet; energy restricted diet versus no energy restricted diet; low-carbohydrate diet versus high-carbohydrate diet; low-GI diet versus high-fibre moderate-GI diet; soy protein-enriched diet versus no soy protein diet; high-fibre diet versus standard-fibre diet; ethnic specific diet versus standard healthy diet; exercise versus control; intensive management versus routine care; or strict intensity of glycaemic control versus less strict glycaemic control.

40.0 Head circumference and z score

Head circumference was reported as an outcome by one review (Han 2017) (Table 2.13; Table 2.19). The review did not report data for head circumference z scores. The quality of the evidence ranged from *moderate- to very low-quality.*

40.1 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for head circumference at birth for babies born to mothers with GDM between the low-moderate GI diet and moderate-high GI diet group (MD 0.40 cm, 95% CI -0.58 to 1.38; one trial, 59 babies; *very low-quality evidence*) (Han 2017).

40.2 DASH diet versus control diet with matching macronutrient contents: The evidence suggested a reduced head circumference at birth for babies born to mothers with GDM in the DASH diet group compared to the diet with matching macronutrient contents group (MD -0.90 cm, 95% CI -1.44 to -0.36; one trial, 52 babies; *moderate-quality evidence*) (Han 2017).

40.3 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for head circumference at birth for babies born to mothers with GDM between the low-GI diet and high-fibre

moderate-GI diet group (MD -0.20 cm, 95% CI -0.91 to 0.51; one trial, 82 babies; *very low-quality evidence*) (Han 2017).

40.4 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for head circumference at birth for babies born to mothers between the soy protein-enriched diet and no soy protein diet group (MD -0.20, 95% CI -1.01 to 0.61; one trial, 68 babies; *very low-quality evidence*) (Han 2017).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed a reduction of head circumference at birth for babies born to mothers with GDM who were treated with the DASH diet compared to the control diet with matching macronutrient contents evidence.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence showed no clear difference for head circumference at birth for babies born to mothers with GDM who were treated with low-moderate GI diet versus moderate-high GI diet; low-GI diet versus high-fibre moderate-GI diet; or soy protein-enriched diet versus no soy protein diet.

41.0 Length and z score

Length at birth was reported as an outcome by three reviews (Brown 2017b; Brown 2017c; Han 2017) (Table 2.13; Table 2.19). There was no clear evidence of a difference for length at birth for any of the comparisons reporting this outcome. The reviews did not report data for length z scores. The quality of the evidence ranged from *low- to very low-quality.*

41.1 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for length at birth for babies born to mothers with GDM between the low-moderate GI diet and moderate-high GI diet group (MD -0.50 cm, 95% CI -1.54 to 0.54; one trial, 60 babies; *very low-quality evidence*) (Han 2017).

41.2 DASH diet versus control diet with matching macronutrient contents: There was no clear difference for length at birth for babies born to mothers between the DASH diet and control diet with matching macronutrient contents group (MD -0.50 cm, 95% CI -1.59 to 0.59; one trial, 52 babies; *low-quality evidence*) (Han 2017).

41.3 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for length at birth for babies born to mothers with GDM between the low-GI diet and high-fibre moderate-GI diet group (MD 0.0 cm, 95% CI -0.83 to 0.83; one trial, 92 babies; *very low-quality evidence*) (Han 2017).

41.4 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for length at birth for babies born to mothers with GDM between the soy protein-enriched diet and no soy protein diet group (MD -0.10 cm, 95% CI -1.07 to 0.87; one trial, 68 babies; *very low-quality evidence*) (Han 2017).

41.5 Lifestyle intervention versus usual care or diet alone: There was no clear difference for length at birth for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (MD -0.10 cm, 95% CI -0.37 to 0.17; one trials, 700 babies; *low-quality evidence*) (Brown 2017b).

41.6 Exercise versus control: There was no clear difference for length at birth for babies born to mothers with GDM between the exercise and control group (MD -1.70 cm, 95% CI -3.41 to 0.01; one trial, 34 babies; *very low-quality evidence*) (Brown 2017c).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for length at birth for babies born to mothers with GDM who were treated with DASH diet versus control diet with matching macronutrient contents; or lifestyle intervention versus usual care or diet alone.
- *Very low-quality* evidence showed no clear difference for length at birth for babies born to mothers with GDM who were treated with low-moderate GI diet versus moderate-high GI diet; low-GI diet versus high-fibre moderate-GI diet; soy protein-enriched diet versus no soy protein diet; or exercise versus control.

42.0 Ponderal index

Ponderal index was reported as an outcome by three reviews (Brown 2017a; Han 2012; Han 2017) Table 2.13; Table 2.19). The quality of the evidence ranged from *moderate- to very low-quality.*

42.1 Metformin versus glibenclamide: The evidence suggested a reduced ponderal index for babies born to mothers with GDM in the metformin group compared to the glibenclamide group (MD -0.09 units, 95% CI -0.17 to -0.01; one trial, 200 babies; *low-quality evidence*) (Brown 2017a).

42.2 Low-moderate GI diet versus moderate-high GI diet: There was no clear difference for the ponderal index at birth for babies born to mothers with GDM between the low-moderate GI diet and moderate-high GI diet group (MD -0.10 kg/m^3, 95% CI -0.03 to 0.23; one trial, 60 babies; *very low-quality evidence*) (Han 2017).

42.3 DASH diet versus control diet with matching macronutrient contents: The evidence suggested a reduced ponderal index at birth for babies born to mothers with GDM in the DASH diet group (MD -0.37 kg/m^3, 95% CI -0.54 to -0.20; one trial, 52 babies; *moderate-quality evidence*) (Han 2017).

42.4 Low-GI diet versus high-fibre moderate-GI diet: There was no clear difference for the ponderal index at birth for babies born to mothers with GDM between the low-GI diet and high-fibre moderate-GI diet group (MD 0.20 kg/m^3, 95% CI -0.79 to 1.19; one trial, 92 babies; *very low-quality evidence*) (Han 2017).

42.5 Intensive management versus routine care: The evidence suggested a reduced ponderal index for babies born to mothers with GDM in the intensive management group (MD -0.09 g x 100 m^3, 95% CI -0.16 to -0.02; one trial, 300 babies; *low-quality evidence*) (Han 2012).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence suggested a benefit of a reduction of ponderal index at birth for babies born to mothers with GDM who were treated with the DASH diet compared to the control diet with matching macronutrient contents evidence. This was less than 0.37 kg/m^3 on average and the babies in this treatment group had also reduced macrosomia as previously reported.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence of a benefit by a small reduction in ponderal index at birth for babies born to mothers with GDM who were treated with intensive management compared to routine care; or metformin compared to glibenclamide.
- *Very low-quality* evidence showed no clear difference for ponderal index at birth for babies born to mothers with GDM who were treated with low-moderate GI diet versus moderate-high GI diet; or low-GI diet versus high-fibre moderate-GI diet.

43.0 Adiposity (including skinfold thickness measurements (mm), fat mass)

Adiposity was reported as an outcome by one review (Brown 2017b). No other measures of adiposity were reported (Table 2.9; Table 2.19). The quality of the evidence was *low-quality.*

43.1 Lifestyle intervention versus usual care or diet alone: The evidence suggested a reduction for whole-body neonatal fat mass (estimated from skinfold thickness) for babies born to mothers with GDM in the lifestyle intervention group compared to the usual care or diet alone group (MD -37.30 g, 95% CI -63.97 g to -10.63 g; one trial, 958 babies; *low-quality evidence*) (Brown 2017b).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit by a reduced whole-body neonatal fat mass for babies born to mothers with GDM who were treated with lifestyle intervention compared to usual care or diet alone. As previous reported there was also a reduction for preterm birth, birthweight and macrosomia for these babies in the treatment group.

44.0 Neonatal hypoglycaemia (as defined in the reviews)

Neonatal hypoglycaemia was reported as an outcome by six reviews (Boulvain 2001; Brown 2016a; Brown 2017a; Brown 2017b; Brown 2017c; Han 2017) (Table 2.9; Table 2.19). The quality of the evidence ranged from *moderate- to very low-quality.* In six reviews there was no definition provided for neonatal hypoglycaemia for specific comparisons and four reviews provided definitions for specific comparisons although these definitions varied.

44.1 Neonatal hypoglycaemia (not defined in the reviews)

44.1.1 Induction of labour versus expectant management: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the induction of labour and expectant management group (RR not estimable; one trial, 200 babies; *very low-quality evidence*) (Boulvain 2001). There were no neonatal hypoglycaemic events in both groups.

44.1.2 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the oral antidiabetic drug glibenclamide and placebo group (RR 1.97, 95% CI 0.36 to 10.62; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

44.1.3 Myo-inositol versus placebo: The evidence suggested a reduced risk of neonatal hypoglycaemia for babies born to mothers with GDM in the myo-inositol group compared with placebo group (RR 0.05, 95% CI 0.00 to 0.85; one trial, 73 babies; *low-quality evidence*) (Brown 2016a).

44.1.4 Energy restricted diet versus no energy restricted diet: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the energy restricted diet and no energy restricted diet group (RR 1.06, 95% CI 0.48 to 2.32; two trials, 408 babies; *very low-quality evidence*) (Han 2017).

44.1.5 Low-carbohydrate diet versus high-carbohydrate diet: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the low-carbohydrate and high-carbohydrate diet group (RR 0.91, 95% CI 0.39 to 2.12; one trial, 149 babies; *very low-quality evidence*) (Han 2017).

44.1.6 Ethnic specific diet versus standard healthy diet: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the ethnic specific diet and standard healthy diet group (RR not estimable; one trial, 20 babies; *very low-quality evidence*). There were no neonatal hypoglycaemic events in both groups (Han 2017).

44.1.7 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (Average RR 0.99, 95% CI 0.65 to 1.52; six trials, 3000 babies; *moderate-quality evidence*) (Brown 2017b).

44.1.8 Exercise versus control: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the exercise and control group (RR 2.00, 95% CI 0.20 to 20.04; one trial, 34 babies; *low-quality evidence*) (Brown 2017c).

44.2 Neonatal hypoglycaemia (defined)

44.2.1 Metformin versus glibenclamide: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the metformin and glibenclamide group (RR 0.86, 95% CI 0.42 to 1.77; four trials, 554 babies; *low-quality evidence*) (Brown 2017a). Hypoglycaemia defined as BGL < 2.2 mmol/L; < 40 mg/dL.

44.2.2 Glibenclamide versus acarbose: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the glibenclamide and acarbose group (RR 6.33, 95% CI 0.87 to 46.32; one trial, 43 babies; *low-quality evidence*) (Brown 2017a). Hypoglycaemia defined as BGL < 2.2 mmol/L; < 40 mg/dL.

44.2.3 Soy protein-enriched diet versus no soy protein diet: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the soy protein-enriched diet and no soy protein diet group (RR 3.00, 95% CI 0.33 to 27.42; one trial, 68 babies; *very low-quality evidence*) (Han 2017). Hypoglycaemia defined as BGL < 1.7 mmol/L (< 30.6 mg/dL).

44.2.4 Intensive management versus routine care: There was no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM between the intensive management and routine care group (RR 0.39, 95% CI 0.06 to 2.54; two trials, 426 babies; *very low-quality evidence*) (Han 2012). Hypoglycaemia defined in one trial as BGL < 1.7 mmol/L in two consecutive measurements and as BGL < 1.94 mmol/L in the other trial.

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed no clear difference for the risk of neonatal hypoglycaemia (not defined) for babies born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested a benefit by a reduced risk of neonatal hypoglycaemia for babies born to mothers with GDM who were treated with myo-inositol versus placebo (hypoglycaemia not defined).
- *Low-quality* evidence showed no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM who were treated with metformin versus glibenclamide; or glibenclamide versus acarbose (hypoglycaemia defined) or were treated with exercise versus control (hypoglycaemia not defined).
- *Very low-quality* evidence showed no clear difference for the risk of neonatal hypoglycaemia for babies born to mothers with GDM who were treated with soy protein-enriched diet versus no soy protein diet; or intensive management versus routine care evidence (hypoglycaemia defined) or were treated with induction of labour versus expectant management; glibenclamide versus placebo; energy restricted diet versus no energy restricted diet; low-carbohydrate diet versus high-carbohydrate diet; or ethnic specific diet versus standard healthy diet (hypoglycaemia not defined).

45.0 Respiratory distress syndrome (RDS)

RDS was reported as an outcome by five reviews (Boulvain 2001; Brown 2017a; Brown 2017b; Brown 2017c; Han 2017) (Table 2.13; Table 2.19). There was no clear evidence of a difference for RDS for any of the comparisons reporting this outcome. The quality of the evidence ranged from *moderate- to very low-quality.* Only one review provided a definition of RDS.

45.1 Induction of labour versus expectant management: There were no RDS (termed neonatal asphyxia in the review) events reported in either group. for babies born to mothers with GDM between the induction of labour and expectant management group (RR not estimable; one trial, 200 babies; *very low-quality evidence*) (Boulvain 2001).

45.2 Metformin versus glibenclamide: There was no clear difference for the risk of RDS for babies born to mothers with GDM between the metformin and glibenclamide group (RR 0.51, 95% CI 0.10 to 2.69; one trial, 159 babies; *very low-quality evidence*) (Brown 2017a).

45.3 Glibenclamide versus acarbose: There were no RDS events reported in either group for babies born to mothers with GDM between the glibenclamide and acarbose group (RR not estimable; one trial, 43 babies; *low-quality evidence*) (Brown 2017a).

45.4 Ethnic specific diet versus standard healthy diet: There were no RDS events reported in either group for the risk of RDS for babies born to mothers with GDM between the ethnic specific diet and standard healthy diet group (RR not estimable; one trial, 20 babies; *low-quality evidence*) (Han 2017).

45.5 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of RDS for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (average RR 0.79, 95% CI 0.34 to 1.85; four trials, 2195 babies; *moderate-quality evidence*) (Brown 2017b).

45.6 Exercise versus control: There were no RDS events reported in either group for babies born to mothers with GDM between the exercise and control group (RR not estimable; one trial, 34 babies; *very low-quality evidence*) (Brown 2017c).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed no clear difference for the risk of RDS for babies born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence reported no events of RDS in either group for babies born to mothers with GDM who were treated with glibenclamide versus acarbose; or ethnic specific diet versus standard healthy diet.

Summary

- *Very low-quality* evidence showed no clear difference for the risk of RDS for babies born to mothers with GDM who were treated with induction of labour versus expectant management (no events); metformin versus glibenclamide; or exercise versus control (no events).

46.0 Neonatal jaundice (hyperbilirubinaemia) (as defined in the reviews)

Neonatal jaundice (hyperbilirubinaemia) was reported as an outcome by five reviews (Brown 2017a; Brown 2017b; Brown 2017c; Han 2012; Han 2017 (Table 2.13; Table 2.19). Only one of the included reviews reporting this outcome provided a definition for neonatal jaundice. The quality of the evidence ranged from *moderate- to very low-quality.*

46.1 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of neonatal jaundice for babies born to mothers with GDM between the glibenclamide and placebo group (RR 1.97, 95% CI 0.50 to 7.75; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

46.2 Metformin versus glibenclamide: There was no clear difference for the risk of neonatal jaundice for babies born to mothers with GDM between the metformin and glibenclamide group (RR 0.68, 95% CI 0.37 to 1.25; two trials, 1205 babies; *moderate-quality evidence*) (Brown 2017a).

46.3 Energy restricted diet versus no energy restricted diet: There was no clear difference for the risk of neonatal jaundice for babies born to mothers with GDM between the energy restricted diet and no energy restricted diet group (RR 0.81, 95% CI 0.33 to 1.98; one trial, 299 babies; *low-quality evidence*) (Han 2017).

46.4 Soy protein-enriched diet versus no soy protein diet: The evidence suggested a reduced risk of neonatal jaundice for babies born to mothers with GDM in the soy protein-enriched diet group compared to the no soy protein diet group (RR 0.27, 95% CI 0.08 to 0.89; one trial, 68 babies; *very low-quality evidence*) (Han 2017).

46.5 Ethnic specific diet versus standard healthy diet: There were no events of neonatal jaundice for babies born to mothers with GDM in the ethnic specific diet or the standard healthy diet group (RR not estimable; one trial, 20 babies; *low-quality evidence*) (Han 2017).

46.6 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of neonatal jaundice for babies born to mothers with GDM between the lifestyle intervention and usual

care or diet alone group (average RR 0.76, 95% CI 0.50 to 1.16; four trials, 2362 babies; *moderate-quality evidence*) (Brown 2017b).

46.7 Exercise versus control: There was no clear difference for the risk of neonatal jaundice for babies born to mothers with GDM between the exercise and control group (RR 0.33, 95% CI 0.01 to 7.65; one trial, 34 babies; *very low-quality evidence*) (Brown 2017c). There were no events of neonatal jaundice in the intervention group and one event in the control group.

46.8 Intensive management versus routine care: There was no clear difference for the risk of neonatal jaundice for babies born to mothers with GDM between the intensive management and routine care group (RR 0.79, 95% CI 0.24 to 2.60; two trials, 426 babies; *low-quality evidence*) (Han 2012). Hyperbilirubinaemia was defined in the review from one trial as plasma bilirubin at least 205 µmol/l and as plasma bilirubin at least 670 µmol/l in the other included trial.

Summary

Probably no difference between intervention: the direction of the effect suggest benefit; moderate -quality evidence

- *Moderate-quality* evidence showed no clear difference for the risk of neonatal jaundice for babies born to mothers with GDM who were treated with metformin versus glibenclamide (not defined); or lifestyle intervention versus usual care or diet alone (not defined).

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence of benefit showed a lower risk of neonatal jaundice for babies born to mothers with GDM who were treated with soy protein-enriched diet compared to no soy protein diet (not defined).
- *Low-quality* evidence showed no clear difference for the risk of neonatal jaundice for babies born to mothers with GDM who were treated with energy restricted diet versus no energy restricted diet (not defined); ethnic specific diet versus standard healthy diet (not defined) (no events); or intensive management versus routine care (for definition see under heading: effects of interventions page 41.
- *Very low-quality* evidence showed no clear difference for the risk of neonatal jaundice for babies born to mothers with GDM who were treated with glibenclamide versus placebo (not defined); or exercise versus control (not defined).

47.0 Hypocalcaemia

Hypocalcaemia was reported as an outcome by three reviews (Brown 2017b; Brown 2017c; Han 2017) (Table 2.13; Table 2.19). None of the included reviews reporting this outcome provided a definition for hypocalcaemia. The quality of the evidence ranged from *moderate- to very low-quality.*

47.1 Energy restricted diet versus no energy restricted diet: The evidence suggested an increased risk of hypocalcaemia for babies born to mothers with GDM in the energy restricted diet group compared to the no energy restricted diet group (RR 1.36, 95% CI 1.00 to 1.86; one trial, 299 babies; *low-quality evidence*) (Han 2017).

47.2 Ethnic specific diet versus standard healthy diet: There were no events of hypocalcaemia reported for babies born to mothers with GDM in the ethnic specific diet or the standard healthy diet group (RR not estimable; one trial, 20 babies; *low-quality evidence*) (Han 2017).

47.3 Lifestyle intervention versus usual care or diet alone: The evidence suggested an increased risk of hypocalcaemia for babies born to mothers with GDM in the lifestyle intervention group compared to the usual care or diet alone group (RR 1.38, 95% CI 1.01 to 1.88; two trials, 462 babies; *moderate-quality evidence*) (Brown 2017b).

47.4 Exercise versus control: There were no events of hypocalcaemia reported for babies born to mothers with GDM in the exercise or the control group (RR not estimable; one trial, 34 babies; *very low-quality evidence*) (Brown 2017c).

Summary

Probably ineffective interventions: moderate-quality of evidence suggesting lack of effectiveness, more evidence needed

- *Moderate-quality* evidence of harm showed an increased risk of hypocalcaemia for babies born to mothers with GDM who were treated with lifestyle intervention compared to usual care or diet alone.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence suggested harm by an increased risk of hypocalcaemia for babies born to mothers with GDM who were treated with energy restricted diet versus no energy restricted diet.
- *Low-quality* evidence reported no events of hypocalcaemia for babies born to mothers with GDM who were treated with ethnic specific diet versus standard healthy diet.
- *Very low-quality* evidence reported no events of hypocalcaemia for babies born to mothers with GDM who were treated with exercise versus control.

48.0 Polycythaemia

Polycythaemia was reported as an outcome by one review (Brown 2017b) (Table 2.13). The review did not provide a definition of polycythaemia. The quality of the evidence was low-quality.

48.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of polycythaemia for babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (RR 0.22, 95% CI 0.01 to 5.40; one trial, 165 babies; *low-quality evidence*) (Brown 2017b). There was one case of polycythaemia in the control group.

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for the risk of polycythaemia for babies born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone.

Secondary outcomes - Later infant/childhood

49.0 Weight and z scores

Weight in later childhood was reported as an outcome by one review (Brown 2017b) (Table 2.14; Table 2.19). The included review did not report data for weight z scores in the later infant/childhood. The quality of the evidence was *low-quality.*

49.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for childhood weight (at four to five years of age) for children born to mothers who had GDM between the lifestyle intervention and usual care or diet alone group (MD -0.30 kg, 95% CI -1.29 to 0.69; one trial, 199 children; *low-quality evidence*) (Brown 2017b).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference in weight for children born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone at four to five years of age.

50.0 Height and z scores

Height in later childhood was reported as an outcome by one review (Brown 2017b) (Table 2.14; Table 2.19). The included review did not report data for height z scores in the later infant/childhood. The quality of the evidence was *low-quality.*

50.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for childhood height (at four to five years of age) for children born to mothers who had GDM between the

lifestyle intervention and usual care or diet alone group (MD -0.60 cm, 95% CI -2.05 to 0.85; one trial, 199 children; *low-quality evidence*) (Brown 2017b).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference in height for children born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone at four to five years of age.

51.0 Adiposity (including BMI, skinfold thickness, fat mass)

Adiposity was reported as an outcome by one review (Brown 2017b) (Table 2.9; Table 2.19). The included review did not report data for skinfold thickness or fat mass in the later infant/childhood. The quality of the evidence ranged from *moderate- to very low-quality.*

51.1 Childhood BMI

51.1.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for childhood BMI > 85th percentile (at four to five years follow-up in one trial, seven to 11 years follow-up in the second included trial and five to ten years follow-up in the third trial) for children born to mothers who had GDM between the lifestyle intervention and usual care or diet alone group (RR 0.91 kg/m^2, 95% CI 0.75 to 1.11; three trials, 767 children; *moderate-quality evidence*) (Brown 2017b).

51.1.2 Childhood BMI z score

Lifestyle intervention versus usual care or diet alone: There was no clear difference for childhood BMI z score (at four to five years follow-up) for children born to mothers who had GDM between the lifestyle intervention and usual care or diet alone group (MD 0.08, 95% CI -0.28 to 0.44; one trial, 199 children; *very low-quality evidence*) (Brown 2017b).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed no clear difference for childhood BMI for children born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone at four to five years of age (one trial), seven to 11 years of age (one trial) or five to 10 years of age (one trial).

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence showed no clear difference in childhood BMI z score for children born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone at four to five years of age.

52.0 Blood pressure

Blood pressure was reported as an outcome in one review (Brown 2017b). The review reported no clear evidence of a difference in systolic or diastolic blood pressure from a single trial in children (at five to 10 years follow-up) whose mothers with GDM were treated with either a lifestyle intervention or usual care (*moderate-quality evidence*). The data in the on included trial was not in a format suitable for inclusion in a meta-analysis.

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed no clear difference for childhood blood pressure for children born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone at five to 10 years of age.

53.0 Impaired glucose tolerance

Impaired glucose tolerance was reported as an outcome in the later infant/childhood by one review (Brown 2017b) (Table 2.14; Table 2.19). The quality of the evidence was *low-quality.* Data were reported as fasting blood glucose and two-hour post-prandial blood glucose.

53.1 Impaired glucose tolerance: fasting blood glucose

53.1.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for impaired glucose tolerance (at seven to 11 years of age) for children born to mothers who had GDM between the lifestyle intervention and usual care or diet alone group (MD 0.10 mmol/L, 95% CI -0.10 to 0.30; one trial, 68 children; *low-quality evidence*) (Brown 2017b).

53.2 Impaired glucose tolerance: two-hour post-prandial blood glucose

53.2.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for impaired glucose tolerance (at seven to 11 years follow-up) for children born to mothers between the lifestyle intervention and usual care or diet alone group (MD 0.00 mmol/L, 95% CI -0.48 to 0.48; one trial, 68 children; *low-quality evidence*) (Brown 2017b).

One further included trial in the (Brown 2017b) review reported data for impaired glucose tolerance in children (at five to 10 years follow-up). The data could not be combined in a meta-analysis.

Summary

No conclusions possible: low- to very low quality-evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference at fasting or two-hour post-prandial blood glucose for children born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone at seven to 11 years of age.

54.0 Dyslipidaemia or metabolic syndrome

Dyslipidaemia or metabolic syndrome (total, LDL and HDL cholesterol) was reported as an outcome by one review (Brown 2017b). There were no data reported for metabolic syndrome (Table 2.14; Table 2.19). The quality of the evidence was *low-quality.*

54.1 Dyslipidaemia or metabolic syndrome: Total cholesterol

54.1.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for total cholesterol concentration (at seven to 11 years follow-up) for children born to mothers who had GDM between the lifestyle intervention and usual care or diet alone group (MD -0.20 mg/dL, 95% CI -0.55 to 0.15; one trial, 68 children; *low-quality evidence*) (Brown 2017b).

54.2 Dyslipidaemia or metabolic syndrome: LDL cholesterol

54.2.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for LDL cholesterol concentration (at seven to 11 years follow-up) for children born to mothers who had GDM between the lifestyle intervention and usual care or diet alone group (MD -0.12 mg/dL, 95% CI -0.50 to 0.26; one trial, 68 children; *low-quality evidence*) (Brown 2017b).

54.3 Dyslipidaemia or metabolic syndrome: HDL cholesterol

54.3.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for HDL cholesterol concentration (at seven to 11 years follow-up) for children born to mothers who had GDM between the lifestyle intervention and usual care or diet alone group (MD 0.10 mg/dL, 95% CI -0.05 to 0.25; one trial, 68 children; *low-quality evidence*) (Brown 2017b).

One included trial in the (Brown 2017b) review reported data for HDL cholesterol concentration (low) and triglyceride concentration (elevated) in children (at five to 10 years follow-up). The data could not be combined in a meta-analysis. Another included trial reported data for triglyceride concentration in children (at seven to 11 years follow-up) with no clear difference between lifestyle intervention versus usual care or diet alone group and not published as a meta-analysis.

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for total cholesterol, LDL cholesterol or HDL cholesterol for children born to mothers with GDM who were treated with lifestyle intervention versus usual care or diet alone at seven to 11 years of age.

55.0 Pre-specified overview child as later infant/childhood secondary outcomes not reported in the included reviews

None of the included reviews reported any data for the child as later infant/childhood secondary overview outcomes: head circumference and z scores, educational attainment, development of type 1 diabetes and development of type 2 diabetes.

Secondary outcomes - Child as an adult

None of the included reviews reported any data for the child as an adult for the following secondary overview outcomes: weight and z scores, height and z scores, adiposity (including BMI, skinfold thickness, fat mass), blood pressure, employment, education and social status/achievement, dyslipidaemia or metabolic syndrome, development of type 1 diabetes, development of type 2 diabetes and impaired glucose tolerance.

Secondary outcomes - Health service use

56.0 Number of antenatal visits or admissions

The number of antenatal visits or admissions was reported as an outcome by two reviews (Brown 2017b; Han 2017) (Table 2.10; Table 2.19). The quality of the evidence ranged from *moderate- to very low-quality.*

56.1 Soy protein-enriched diet versus no soy protein diet: There was no clear difference in the number of antenatal visits or admissions (defined as maternal hospitalisation) for women with GDM in the soy protein-enriched diet and no soy protein diet group (RR 0.75, 95% CI 0.18 to 3.10; one trial, 68 women; *very low-quality evidence*) (Han 2017).

56.2 Lifestyle intervention versus usual care or diet alone: There was no clear difference in the number of antenatal visits or admissions (not defined) for women with GDM between the lifestyle intervention and usual care or diet alone group (RR 1.06, 95% CI 0.87 to 1.29; one trial, 1000 women; *moderate-quality evidence*) (Han 2017).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence showed no clear difference in number of antenatal visits or admissions for health service use for women with GDM who were treated with soy protein-enriched diet versus no soy protein diet.

57.0 Number of hospital or health professional visits (including midwife, obstetrician, physician, dietitian, diabetic nurse)

Number of hospital or health professional visits was reported as an outcome by one review (Brown 2017b) (Table 2.15; Table 2.19). The review reported data for visits with a dietitian, diabetes educator, obstetrician and non-specified health professional. The quality of the evidence ranged from *moderate- to low-quality.*

57.1 Visits with dietitian

57.1.1 Lifestyle intervention versus usual care or diet alone: The evidence suggested an increase for the number of visits with a dietitian for women with GDM in the lifestyle intervention group compared

to the usual care or diet alone group (RR 9.24, 95% CI 7.12 to 12.01; one trial, 1000 women; *moderate-quality evidence*) (Brown 2017b).

57.2 Visits with diabetes educator

57.2.1 Lifestyle intervention versus usual care or diet alone: The evidence suggested an increase for the number of visits with a diabetes educator for women with GDM in the lifestyle intervention group compared to the usual care or diet alone group (RR 8.55, 95% CI 6.67 to 10.96; one trial, 1000 women; *moderate-quality evidence*) (Brown 2017b).

57.3 Visits with obstetrician

57.3.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the number of visits with an obstetrician for women with GDM between the lifestyle intervention and usual care or diet alone group (MD 0.20 visits, 95% CI -0.21 to 0.61; one trial, 700 women; *low-quality evidence*) (Brown 2017b).

57.4 Visits with healthcare provider (not specified)

57.4.1 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the number of visits with a healthcare provider (not specified) for women with GDM between the lifestyle intervention and usual care or diet alone group (MD 0.10 visits, 95% CI -1.58 to 1.78; one trial, 197 women; *low-quality evidence*) (Brown 2017b).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence of an increased number of antenatal visits with a **dietitian** and **diabetes educator** for women with GDM who were treated with lifestyle intervention compared to usual care or diet alone. This would be expected as the intervention requires close surveillance.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference in number of antenatal visits with an **obstetrician** and **other health providers** (not defined) for women with GDM who were treated with lifestyle intervention versus usual care or diet alone.

58.0 Admission to neonatal intensive care unit/nursery

Admission to the neonatal intensive care unit/nursery (NICU) was reported as an outcome by four reviews (Brown 2017a; Brown 2017b; Han 2012; Han 2017) (Table 2.15; Table 2.19). There was no clear evidence of a difference for the risk of admission to NICU for any of the comparisons reporting this outcome. The quality of the evidence ranged from *moderate- to very low-quality.*

58.1 Oral antidiabetic agents versus placebo: There was no clear difference for the risk of admission to NICU for the babies born to mothers with GDM between the oral antidiabetic drug glibenclamide and placebo group (RR 1.16, 95% CI 0.53 to 2.53; one trial, 375 babies; *very low-quality evidence*) (Brown 2017a).

58.2 Metformin versus glibenclamide: There was no clear difference for the risk of admission to NICU for the babies born to mothers with GDM between the metformin and glibenclamide group (RR 1.52; 95% CI 0.65 to 3.56; two trials, 349 babies; *low-quality evidence*) (Brown 2017a).

58.3 Soy protein-enriched diet versus no soy protein diet: There was no clear difference of admission to NICU for babies born to mothers with GDM in the soy protein-enriched diet and no soy protein diet group (RR 0.14, 95% CI 0.02 to 1.10; one trial, 68 women; *very low-quality evidence*) (Han 2017). (Admission was defined as "hypoxia, low-risk Apgar scores 6-7 (at 5 or 15 min of age), high-risk Apgar scores at 1 minute 0-5 and at 5 or 15 minutes less than 6, hyperbilirubinaemia, birth weight less than 2500 g, and/or gestational age less than 32 weeks, sepsis, pneumonia, or meningitis, hypoglycaemia (blood glucose < 1.7mmol/L")).

58.4 Intensive management versus routine care: There was no clear difference for the risk of admission to NICU for the babies born to mothers with GDM between the intensive management and routine care group (RR 0.64, 95% CI 0.29 to 1.45; two trials, 426 babies; *moderate-quality evidence*) (Han 2012).

58.5 Lifestyle intervention versus usual care or diet alone: There was no clear difference for the risk of admission to NICU for the babies born to mothers with GDM between the lifestyle intervention and usual care or diet alone group (Average RR 0.91, 95% CI 0.59 to 1.40; three trials, 2030 women; *low-quality evidence*) (Brown 2017b).

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence showed no clear difference for admission to neonatal intensive care unit/nursery for babies born to mothers with GDM who were treated with intensive management versus routine care.

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Low-quality* evidence showed no clear difference for admission to neonatal intensive care unit/nursery for babies born to mothers with GDM who were treated with metformin versus glibenclamide; or lifestyle intervention versus usual care or diet alone.
- *Very low-quality* evidence showed no clear difference for admission to neonatal intensive care unit/nursery for babies born to mothers with GDM who were treated with glibenclamide agents versus placebo; or soy protein-enriched diet versus no soy protein diet.

59.0 Length of postnatal stay (baby)

Length of postnatal stay was reported as an outcome by one review (Han 2017) (Table 2.10; Table 2.10). The quality of the evidence was *very low-quality evidence.*

59.1 Diet recommendation + diet-related behavioural advice versus diet recommendation only: There was no clear difference in length of postnatal stay (defined as more than four days) for babies born to mothers with GDM between the diet recommendation + diet-related behavioural advice and diet recommendation only group (RR 1.33, 95% CI 0.73 to 2.44; one trial, 99 babies; *very low-quality evidence*) (Han 2017).

Summary

No conclusions possible: low- to very low-quality evidence, or insufficient evidence to comment on the effectiveness, more evidence needed

- *Very low-quality* evidence showed no clear difference for length of postnatal stay for babies born to mothers with GDM who were treated with diet recommendation + diet-related behavioural advice versus diet recommendation only.

60.0 Costs associated with the treatment

Costs associated with the treatment was reported as an outcome by one review (Brown 2017b) (Table 2.20).

60.1 Lifestyle intervention versus usual care or diet alone: *Moderate-quality* evidence showed costs (in AUD) were higher for women with mild GDM and a singleton pregnancy in the lifestyle intervention group compared to the usual care or diet alone group, which was mainly due to increased surveillance

and increased contact with health professionals (one trial, 1000 women) (Brown 2017b). The data were reported as direct costs per 100 women, but were not in a suitable format for inclusion in a meta-analysis and are summarised in (Table 2.20)

Summary

Promising interventions: moderate-quality evidence of effectiveness, more evidence needed

- *Moderate-quality* evidence suggested increased total costs of approximately AU$33,00 associated with the treatment and of approximately AU$ 6,000 associated costs for the families of women with GDM who were treated with lifestyle intervention compared to usual care or diet alone (Table 18). This was mainly due to increased surveillance and increased contact with health professionals. The table was reprinted with permission from the Brown 2017b review.

Table 2.20: Costs associated with the treatment

Crowther 2005	Lifestyle intervention	Usual care
Package of treatment for mild GDM versus usual care		
Direct costs per 100 women with a singleton pregnancy - including antenatal clinic visits, specialist clinics, dietician, diabetes educator, insulin therapy	AUD67,432	AUD33,681
In-patient costs - hospital costs	AUD545,125	AUD524,891
Total direct health service costs	AUD612,557	AUD558,572
Patient/family costs	AUD36,749	AUD30,229

Permission granted from John Wiley & Sons, Ltd. to use this treatment costs table from Brown 2017b (table 11, p. 127).

61.0 Pre-specified overview health service use outcomes not reported in the included reviews

None of the included reviews reported data for the following health services use secondary overview outcomes: length of stay in neonatal intensive care unit or special care baby unit, length of antenatal stay, length of postnatal stay (maternal), cost of maternal care, cost of neonatal/child/adult care and costs to families associated with the treatment (e.g. change of diet, extra antenatal visits, etc).

2.2.5 Discussion

Summary of main results

This overview review includes eight Cochrane systematic reviews that reported data about treatments for women with GDM and borderline GDM. These eight Cochrane systematic reviews include 62 RCTs involving 9133 women, 8373 babies and 767 children. RCTs reported in multiple reviews have only been counted as one trial (Brown 2017b and Brown 2017c; Brown 2017b and Han 2017). However, when the

same trial was reported in multiple reviews but with participant numbers from different treatment arms (subsets) they were then counted as one trial each (Han 2017 and Brown 2017c; Han 2012 and Han 2017; Brown 2017b and Brown 2017c).

Data were available from the included reviews for 59 pre-specified overview outcomes of the 80 listed for this overview review. A summary of the main results according to these overview review outcomes, following the framework and its categories as outlined under the heading *Data synthesis* section page 66 and under the heading *Methods* page 54, are presented in Table 2.18 (primary outcomes) and Table 2.19 (secondary outcomes).

We have collated the interventions for treatment of women with GDM, for the GRADE health outcomes of this overview, according to whether they have been found to be effective, promising, probably no difference, ineffective, probably ineffective or no conclusion about effectiveness for health outcomes identified as important for women and their babies:

- Effective interventions: indicating that the review found high-quality evidence of effectiveness for an intervention.
- Promising interventions (more evidence needed): indicating that the review found moderate-quality evidence of effectiveness for an intervention, but more evidence is needed.
- Probably no difference between interventions: direction of effect suggests benefit/harm or ineffective, 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, more evidence needed.

For the mother:

Hypertensive disorders of pregnancy

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing hypertensive disorders of pregnancy.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be promising at reducing hypertensive disorders of pregnancy.

Probably no difference between interventions (more evidence is needed): For metformin compared with glibenclamide there was probably no difference in the rate of hypertensive disorders of pregnancy.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing hypertensive disorders of pregnancy.

Probably ineffective interventions (more evidence needed): The DASH diet was probably ineffective at reducing the rate of hypertensive disorders in pregnancy versus a control diet.

No conclusions possible due to lack of evidence: For the following interventions compared to other interventions, to a control, or to placebo, no conclusion was possible as to the effect on hypertensive disorders of pregnancy: glibenclamide versus placebo; low-moderate GI diet versus moderate-high GI diet; low carbohydrate diet versus high carbohydrate diet; high unsaturated fat diet versus low unsaturated fat diet with matching calories; ethnic specific diet versus standard healthy diet; energy restricted diet versus no energy restricted diet; lifestyle intervention versus usual care or diet alone; exercise versus control; intensive management versus routine care; metformin versus glibenclamide; or soy protein-enriched diet versus no soy protein diet.

Caesarean section

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the risk of birth by caesarean section.

Promising interventions (more evidence needed): The DASH diet and exercise were promising interventions for women with GDM for reducing the risk of birth by caesarean section compared with a control.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for the risk of birth by caesarean section.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing the risk of birth by caesarean section.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the risk of birth by caesarean section.

No conclusions possible due to lack of evidence: For the following interventions compared to other interventions, to a control, or to placebo, no conclusion was possible as to the effect on risk of birth by caesarean section: glibenclamide versus placebo; metformin versus glibenclamide; glibenclamide versus acarbose; energy restricted diet versus no energy restricted diet; low carbohydrate diet versus high-carbohydrate diet; low-GI diet versus high-fibre moderate-GI diet; diet recommendation + diet-related behavioural advice versus diet recommendation only; soy protein-enriched diet versus no soy protein diet; lifestyle intervention versus usual care or diet; low-moderate GI diet versus moderate-high GI diet; high unsaturated fat diet versus low unsaturated fat diet with matching calories; ethnic specific diet versus standard healthy diet; intensive management versus routine care; and strict intensity of glycaemic control versus less strict glycaemic control.

Development of type 2 diabetes

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the risk of development of type 2 diabetes.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be promising at reducing the risk of development of type 2 diabetes.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for the risk of development of type 2 diabetes.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing the risk of development of type 2 diabetes.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the risk of development of type 2 diabetes.

No conclusions possible due to lack of evidence: For the following interventions compared to other interventions, to a control, or to placebo, no conclusion was possible as to the effect on risk of development of type 2 diabetes: lifestyle intervention versus usual care or diet alone; high unsaturated fat diet versus low unsaturated fat diet with matching calories; low-GI diet versus high fibre moderate-GI diet.

Perineal trauma/tearing

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the risk of perineal trauma/tearing.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be promising at reducing the risk of perineal trauma/tearing.

Probably no difference between interventions (more evidence is needed): For lifestyle intervention versus usual care or diet alone there was probably no difference for women with GDM at reducing the risk of perineal trauma/tearing.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing the risk of perineal trauma/tearing.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the risk of perineal trauma/tearing.

No conclusions possible due to lack of evidence: For the following interventions compared to other interventions, to a control, or to placebo, no conclusion was possible as to the effect on risk of perineal trauma/tearing metformin versus glibenclamide or glibenclamide versus placebo.

Postnatal weight retention or return to pre-pregnancy weight

Effective interventions: No treatment interventions for women with GDM were found to be effective at influencing postnatal weight retention or return to pre-pregnancy weight.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be promising at influencing postnatal weight retention or return to pre-pregnancy weight.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for influencing postnatal weight retention or return to pre-pregnancy weight.

Ineffective interventions: Exercise interventions for women with GDM were found to be ineffective for return to pre-pregnancy weight compared with a control.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at influencing postnatal weight retention or return to pre-pregnancy weight.

No conclusions possible due to lack of evidence: For the following interventions compared to other interventions, to a control, or to placebo, no conclusion was possible as to the effect on postnatal weight retention or return to pre-pregnancy weight: lifestyle intervention compared to usual care or diet alone or low-GI diet versus high-fibre moderate-GI diet.

Postnatal depression

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the risk of postnatal depression.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be promising at reducing the risk of postnatal depression.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for the risk of postnatal depression.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing the risk of postnatal depression.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the risk of postnatal depression.

No conclusions possible due to lack of evidence: No conclusion was possible as to the effect on lifestyle intervention compared to usual care or diet alone on postnatal depression.

Induction of labour

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the rates of induction of labour.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be promising at reducing the rates of induction of labour.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for reducing the likelihood of induction of labour.

Ineffective interventions: Lifestyle intervention for women with GDM was found to be ineffective at reducing the rates of induction of labour compared with usual care or diet alone.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the rates of induction of labour.

No conclusions possible due to lack of evidence: For the following interventions compared to other interventions, to a control, or to placebo, no conclusion was possible as to the effect on induction of labour: intensive management compared to the routine care; glibenclamide versus placebo; metformin versus glibenclamide; low-moderate GI diet versus moderate-high GI diet; energy restricted diet versus no energy restricted diet; or exercise versus control.

For the infant/child/adult

Large-for-gestational age (LGA)

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the risk of their baby being born LGA.

Promising interventions (more evidence needed): Lifestyle intervention was found to be a promising intervention for women with GDM for reducing the risk of their infant being born LGA compared to the usual care or diet alone.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for reducing the risk of their baby being born LGA.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing the risk of their baby being born LGA.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the risk of their baby being born LGA.

No conclusions possible due to lack of evidence: For the following interventions compared to other interventions, to a control, or to placebo, no conclusion was possible as to the effect on the risk of their baby being born LGA: induction of labour compared to expectant management at 38 weeks' complete gestation; intensive management compared to routine care; metformin versus glibenclamide; glibenclamide versus acarbose; myo-inositol versus placebo; low-moderate GI diet versus moderate-high GI diet; energy restricted diet versus no energy restricted diet; glibenclamide versus placebo; low carbohydrate diet versus high-carbohydrate diet; high unsaturated fat diet versus low unsaturated fat diet with matching calories; low-GI diet versus high-fibre moderate-GI diet; diet recommendation + diet-related behavioural advice versus diet recommendation only; or ethnic specific diet versus standard healthy diet.

Perinatal (fetal and neonatal death) and later infant mortality

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the risk of perinatal mortality.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be promising at reducing the risk of perinatal mortality.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for reducing the risk of perinatal mortality.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing the risk of perinatal mortality.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the risk of perinatal mortality.

No conclusions possible due to lack of evidence: For the following interventions compared to other interventions, to a control, or to placebo, no conclusion was possible as to the effect on perinatal mortality: glibenclamide versus acarbose; energy restricted diet versus no energy restricted diet; lifestyle intervention versus usual care; diet alone or exercise versus control; induction of labour versus expectant management; metformin versus glibenclamide; or low carbohydrate diet versus high-carbohydrate diet.

Death or serious morbidity composite

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the risk of a neonatal death or serious morbidity composite.

Promising interventions (more evidence needed): Exercise was found to be a promising intervention for women with GDM for reducing the risk a neonatal death or serious morbidity composite compared to control.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for reducing the risk of a neonatal death or serious morbidity composite.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing the risk of a neonatal death or serious morbidity composite.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the risk of a neonatal death or serious morbidity composite.

No conclusions possible due to lack of evidence: For the following interventions compared to other interventions, to a control, or to placebo, no conclusion was possible as to the effect on a neonatal death or serious morbidity composite: metformin versus glibenclamide; ethnic specific diet versus standard healthy diet or with lifestyle intervention versus usual care or diet alone.

Neonatal hypoglycaemia

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the risk of neonatal hypoglycaemia.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be effective at reducing the risk of neonatal hypoglycaemia.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for reducing the risk of neonatal hypoglycaemia.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing the risk of neonatal hypoglycaemia.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the risk of neonatal hypoglycaemia.

No conclusions possible due to lack of evidence: For the following interventions compared to other interventions, to a control, or to placebo, no conclusion was possible as to the effect on neonatal hypoglycaemia: myo-inositol versus placebo; metformin versus glibenclamide; glibenclamide versus acarbose; exercise versus control; soy protein-enriched diet versus no soy protein diet; intensive management versus routine care; induction of labour versus expectant management; glibenclamide versus placebo; energy restricted diet versus no energy restricted diet; low-carbohydrate diet versus high-carbohydrate diet; or ethnic specific diet versus standard healthy diet.

Adiposity (including BMI, skinfold thickness, fat mass)

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the risk of childhood adiposity.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be effective at reducing the risk of childhood adiposity.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for reducing the risk of childhood adiposity.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing the risk of childhood adiposity.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the risk of childhood adiposity.

No conclusions possible due to lack of evidence: No conclusion was possible as to the effect on childhood adiposity for women with GDM who were treated with lifestyle intervention compared with usual care or diet alone.

Development of type 1 diabetes or development of type 2 diabetes

None of the included reviews reported on the outcome of development of type 1 diabetes or development of type 2 diabetes in later childhood or adulthood.

Neurosensory disability in later childhood (as defined in reviews)

None of the included reviews reported on the outcome of neurosensory disability in later childhood.

Health service use

Number of antenatal visits or admissions

Effective interventions: No treatment interventions for women with GDM were found to be effective at influencing the number of antenatal visits or admissions.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be promising at influencing the number of antenatal visits or admissions.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for influencing the number of antenatal visits or admissions.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at influencing the number of antenatal visits or admissions.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at influencing the number of antenatal visits or admissions.

No conclusions possible due to lack of evidence: No conclusion was possible as to the effect on the number of antenatal visits or admission for soy protein-enriched diet versus no soy protein diet.

Length of postnatal stay (mother)

None of the included reviews reported on the outcome of length of postnatal stay for the mother.

Length of postnatal stay (baby)

Effective interventions: No treatment interventions for women with GDM were found to be effective at reducing the length of the infant's postnatal stay.

Promising interventions (more evidence needed): No treatment interventions for women with GDM were found to be promising at reducing the length of the infant's postnatal stay.

Probably no difference between interventions (more evidence is needed): No treatment interventions for women with GDM were found to be equivocal for reducing the length of the infant's postnatal stay.

Ineffective interventions: No treatment interventions for women with GDM were found to be ineffective at reducing the length of the infant's postnatal stay.

Probably ineffective interventions (more evidence needed): No treatment interventions for women with GDM were found to be probably ineffective at reducing the length of the infant's postnatal stay.

No conclusions possible due to lack of evidence: No conclusion was possible as to the effect on the length of postnatal stay (baby) for diet recommendation + diet-related behavioural advice versus diet recommendation only.

Costs to families associated with the treatment, Costs associated with the treatment, cost of maternal care, cost of child (as neonate, child, adult) care.

None of the included reviews reported clear data for the individual on the outcome of costs.

The overall evidence of various interventions for the treatment of women with GDM and their effects on the health of the women and her baby are limited by quantity and quality.

There was some high-quality evidence that exercise interventions for women with GDM were found to be effective for the return to pre-pregnancy weight compared with a control and that lifestyle interventions were ineffective for decreasing the likelihood of induction of labour compared with usual care/diet alone. No other high-quality evidence was found for treatment interventions on the short- or long-term GRADE maternal or neonatal outcomes of this overview.

The available moderate-quality evidence suggests some promising interventions for which more high-quality evidence is needed:

- Exercise compared to control appears to be a promising intervention for reducing a death and serious infant morbidity, but it is difficult to single out which component of the exercises, if any, is the most effective.
- The DASH diet which is rich in fruits, vegetables, whole grains and low-fat dairy products, and low in saturated fats, cholesterol, refined grains and sweets reduced rate of caesarean section.
- Lifestyle interventions reduced the risk of LGA, neonatal hypoglycaemia and childhood BMI. As with the exercise interventions, the lifestyle interventions are multi-component and it is not possible to determine which, if any, components are effective.
- Long-term health outcomes for women and their infants and costs are not well reported.
- Most of the dietary treatments assessed were from interventions reported as single studies that had relatively small numbers of participants, and only a few trials have compared the same or similar dietary interventions.

This overview summarises the evidence from Cochrane systematic reviews of randomised controlled trials for the treatments for women with GDM on relevant health outcomes and may be used by clinicians, clinical guideline developers, consumers, and policymakers to aid decision making to guide clinical practice, health services and future primary research. For further information we suggest

referring to the individual Cochrane systematic reviews for details for the context and components of the interventions.

Overall completeness and applicability of evidence

This overview review summarises published Cochrane systematic reviews of randomised controlled trials of different treatments for women with GDM and the effects on relevant health outcomes. Data were available from the included reviews for 59 pre-specified outcomes of the 80 overview review outcomes. We are aware of two further Cochrane protocols and two title registrations which include treatments for women with GDM such as insulin treatment, home- versus hospital-glucose monitoring, fetal biometry for guiding medical management, planned elective birth, probiotics and Chinese herbal medicines. In future updates of this overview, if these Cochrane systematic reviews have been published, we will assess for eligibility for their inclusion. The evidence of the overview review can be applied to women with GDM in most countries as the trials of the included reviews were conducted in a wide range of countries. Evidence from published or planned Cochrane systematic reviews is still lacking on the use of telemedicine to manage women with GDM and for the use of micronutrients and phytochemicals to treat women with GDM such as cinnamon, zinc, chromium, omega-3 fatty acids and magnesium.

Quality of the evidence

The included Cochrane systematic reviews were assessed with the AMSTAR tool to be of high quality overall (Table 2.16) and assessed with the ROBIS tool to be of low risk of bias overall (Table 2.17).

Six of the eight included Cochrane systematic reviews (Brown 2017a; Brown 2017b; Brown 2017c; Brown 2016a; Han 2017; Martis 2016a) used GRADE to assess for the quality of evidence for agreed GRADE pre-specified outcomes. For Boulvain 2001 and Han 2012 we undertook the GRADE assessments and there are included in (Table 2.8; Table 2.9; Table 2.10). Seven out of the eight included reviews assessed the risk of bias of the included randomised trials, with the majority of reviews following the current guidance as outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). The quality of included randomised trials in these reviews were highly variable within and between the included reviews from high- to very low-quality.

We assessed all the secondary outcomes for this overview using the four GRADE quality ratings for quality of evidence with information accessed from the Risk of Bias tables in the included reviews. The

quality of the randomised trials ranged from high- to very low-quality (Table 2.11; Table 2.12; Table 2.13; Table 2.14; Table 2.15. Evidence was often downgraded for imprecision as evidence was based on one trial with small numbers, with wide confidence intervals and performance bias for not blinding participants and personnel to the intervention, although for many of the interventions being assessed masking of participants and health professionals to the interventions was not possible.

Potential biases in the overview process

We were aware that there were risks of introducing bias at all stages of the overview review process and took steps to minimise this. All included Cochrane systematic reviews used a published protocol that aimed to minimise bias and we similarly developed and published a Cochrane overview protocol (Martis 2016b). A minimum of two overview authors independently assessed Cochrane systematic reviews for inclusion, carried out data extraction and quality assessment, and assessed the quality of the evidence using the ARMSTAR, ROBIS and GRADE approach. One potential source of bias relates to authors of this overview being authors of some of the included reviews. As pre-specified in our protocol, data extraction and quality assessment for these reviews was carried out by two overview authors who were not the review authors.

We undertook a comprehensive search of the Cochrane Database of Systematic Reviews without language or date restrictions, and identified published reviews (Figure 2.1), as well as planned/ongoing reviews (title registrations/protocols) (Table 2.4). While the included reviews were judged to be of moderate (one review) to high quality (seven reviews) and unclear (one review) to low risk of bias (seven reviews), two included reviews were not considered 'up-to-date'. It is possible that additional trials assessing elective delivery management for women with GDM and interventions for women with hyperglycaemia not meeting gestational diabetes diagnostic criteria have been published, but are not yet included in the relevant Cochrane systematic reviews. Furthermore, recent trials for treatments for women with GDM may have been conducted but not yet published. Once published the trials may be included in the relevant Cochrane systematic reviews. Such new evidence will be considered for inclusion in an update of this overview.

One included review (Boulvain 2001) assessed interventions for elective delivery versus expectant management for women diagnosed with pre-gestational diabetes or GDM together. The data could not be separated out for the two different groups. We agreed to include this review as the majority of the results were based on 187 (93.5 %) women with GDM with only 13 (6.5 %) women having pre-

gestational diabetes (defined as type 1 and type 2 diabetes). Potentially this could bias the results of the overview review for elective delivery for women with GDM. In future up-dates of this review the results for women with GDM and women with pre-gestational diabetes. These data can be considered for revision in an update of this overview. Once this included review is up-dated with the separation for women with GDM and women with pre-gestational diabetes it will be incorporated into this overview review at its next up-date.

One included review (Han 2012) assessed interventions for women with hyperglycaemia not meeting gestational diabetes and type 2 diagnostic criteria. We agreed to include the review into this overview review, as different countries have different diagnostic levels for confirming that a pregnant woman has GDM. It is highly possible that women with hyperglycaemia identified in one country as not meeting the gestational diagnostic threshold for GDM would be diagnosed as having GDM in another country. However, this could be a potential bias for over reporting results.

Agreements and disagreements with other studies or reviews

We did not identify any other overview of Cochrane systematic reviews or Cochrane systematic reviews assessing treatments for women with GDM.

2.2.6 Authors' conclusions

Implications for practice

The overall evidence from a range of interventions for the treatment of women with GDM and their effects on the health of the women and her baby is limited by quantity and quality. There is insufficient high-quality evidence about the effects on health outcomes of relevance for women with GDM and their babies for many of the comparisons in this overview comparing treatment interventions for women with GDM.

Lifestyle interventions that include advice on diet and physical activity have become the mainstay of treatment and are recommended in many national clinical practice guidelines. Most dietary treatments assessed are from interventions reported as single studies, with small number of participants, and only a few trials have compared the same or similar dietary interventions.

High quality evidence suggested that lifestyle interventions were ineffective for reducing the likelihood of induction of labour compared with usual diet/diet alone and that exercise compared with control was

ineffective in improving the return to pre-pregnancy weight. However, many of the lifestyle and exercise interventions are multi-component and identifying which of any of the individual components are effective or not effective is not possible with the evidence currently available. No other high-quality evidence was found for any of the other GDM treatment interventions on the short- or long-term GRADE maternal or neonatal outcomes of this overview.

The available evidence suggests some promising interventions for which more high-quality evidence is needed: Lifestyle interventions (reduced risk of LGA); exercise (reduced death and serious infant morbidity); and the DASH diet (reduced rate of caesarean section). Lifestyle interventions, exercise, and considering the DASH diet may be useful for some women with GDM as treatment interventions with or without additional pharmacotherapy with appropriate advice and/or supervision from a health professional.

Long-term health outcomes for women and their infants and costs are not well reported.

For further information we suggest referring to the individual Cochrane systematic reviews for details on the context and components of the interventions.

Implications for research

This overview review highlights that there is insufficient evidence to make conclusions on the effects on relevant health outcomes for many treatments for women with GDM.

High-quality research is required to identify the most effective components or combination of components in lifestyle and exercise interventions. Further high-quality research with appropriate sample size is required using the DASH diet to confirm its effectiveness for improving short-and long-term maternal and infant outcomes.

Other dietary interventions may also be beneficial, but any effect is currently difficult to identify because of the multiple comparisons, small sample sizes and quantity of trials.

Further research should be sufficiently powered to enable important differences in relevant core clinical outcomes, identified in this overview, for women with GDM and their infants to be detected. Outcomes should include long-term outcomes and the costs for treatments, family and service costs.

2.2.7 Plain language summary

Treatments to improve pregnancy outcomes for women who develop diabetes during pregnancy, known as gestational diabetes mellitus: an overview of Cochrane systematic reviews

What is the issue?

Gestational diabetes mellitus (GDM) is a condition that may occur in the second half of the pregnancy when blood glucose control is more difficult to achieve, and a woman develops high blood glucose levels (hyperglycaemia). This may adversely affect the woman and her baby's health. For the women there may be an increased risk of developing high blood pressure and protein in the urine (pre-eclampsia), postnatal depression, or needing a caesarean section. Long term, women are at higher risk of developing type 2 diabetes and heart disease and stroke (cardiovascular disease) later in life. Babies born to mothers with poorly treated GDM are at increased risk of being too large, having low blood glucose (hypoglycaemia) after birth, and yellowing of the baby's skin and eyes (jaundice). Long term, children are at higher risk of being overweight and developing type 2 diabetes.

Why is this important?

Several Cochrane systematic reviews assess different treatments for women with GDM. This makes it difficult for consumers, clinicians, and guideline developers to easily interpret the available information. This Overview of Cochrane systematic reviews provides a one-stop resource summary of the effects for each treatment on the health outcomes for mothers and babies. This may simplify clinical treatment decision-making and assist with the process of guideline development.

What evidence did we find?

We searched the Cochrane Database of Systematic Reviews (28.06.17) for reviews and identified a total of eight Cochrane systematic reviews assessing the treatments for women with GDM. We identified a total of eight systematic reviews which provided data that could be used in this overview. They included 62 RCTs and a total of 9133 women, 8373 babies and 767 children.

We found that there was probably no difference (moderate-quality evidence) between the oral hypoglycaemic drugs metformin and glibenclamide in the number of women with high blood pressure disorders of pregnancy associated with GDM, compared with usual care or diet alone; nor in the risk of perineal tearing when women followed a lifestyle program. Keeping to the DASH (Dietary Approaches to Stop Hypertension) diet, which involves eating more fruits and vegetables, whole grains rather than

refined grains, fat-free or low-fat dairy products and lean protein sources like fish, poultry and bean, did not clearly reduce the risk of having to give birth by caesarean section, and appeared ineffective at reducing the number of women with high blood pressure disorders of pregnancy.

High quality evidence showed lifestyle interventions for women with GDM compared with usual care/diet alone did not reduce the need for induction of labour and exercise interventions for women with GDM were found to be ineffective for the return to pre-pregnancy weight after the birth compared with a control intervention.

For the babies (moderate-quality evidence) lifestyle programs were promising for reducing the risk of the baby being born large for its gestational age compared with usual care or diet alone.

Conclusions on other outcomes were not possible because of low- or very-low quality evidence, or outcomes not being reported in the identified trials.

Several interventions that were supported with moderate-quality evidence that improved one or more of the GRADE health outcomes for this overview. These included the DASH diet and lifestyle interventions. However, further research is needed to assess the effectiveness of these interventions.

What does this mean?

The current evidence for effective interventions for treating women with GDM is limited by the number and sample sizes of randomised controlled trials and the quality of the available evidence. Further high-quality research is needed to identify effective interventions. Some of the interventions had several parts to them such as diet and exercise and education and it was not possible for us to find out which part of the intervention was the most effective.

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As part of the pre-publication editorial process, the protocol was commented on by three peers (an editor and two referees who are external to the editorial team), a member of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

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Contributions of authors

Julie Brown (JB) and Caroline Crowther (CAC) conceived the idea for this overview. Ruth Martis (RM) wrote the first draft of the protocol. Caroline A. Crowther (CAC) and JB provided feedback for all draft protocol versions. Jane Alsweiler (JA) and Michelle R. Downie (MRD) provided feedback for the final protocol.

Emily Shepherd (ES) joined the author team for the review. As some of the overview authors were involved as authors in potential Cochrane systematic reviews considered for inclusion, a spread sheet was created to clearly identify which overview review authors would assess for review eligibility, carry out data extractions and assessments. RM was involved with six reviews, ES with five reviews, JB with two reviews, JA with two reviews and MRD with one review.

RM prepared the first draft of the review. RM and JB prepared the initial summary of results. All authors commented on drafts of the review and the final version of the overview.

Declarations of interest

Ruth Martis, Julie Brown, Emily Shepherd, Jane Alsweiler and Caroline A. Crowther have been involved as authors or co-authors of Cochrane systematic reviews that are included in this overview review. Overview review authors not involved in those reviews assessed the eligibility for inclusion of these reviews.

Caroline A Crowther, Jane Alsweiler and Julie Brown are lead investigators for a randomised controlled trial of tighter glycaemic targets for women with gestational diabetes. This trial is ongoing and not included in the systematic review included in this overview.

Caroline A Crowther was the lead investigator for the ACHOIS trial that assessed treatment for women with mild gestational diabetes. This trial is reported within an included review. She was not involved in the decision about including this review into this overview, nor involved in any data extraction related to that review.

Michelle R Downie has received honorarium for lectures and partial sponsorship to attend conferences from Novo Nordisk and Sanofi Aventis.

Differences between published protocol (Martis 2016b) and review

There are some differences between the published protocol and this review.

Quality assessment of included reviews

Additionally, to the ARMSTAR and the GRADE methodological quality instruments we further assessed the risk of bias of each included Cochrane systematic reviews with ROBIS (**R**isk **O**f **B**ias **I**n **S**ystematic reviews) (Whiting 2016).

We reported the statistical summary by outcomes for clarity, not by interventions as stated in the protocol.

After further discussion during the review writing process, the overview review authors decided that *all* secondary outcomes needed to be assessed for quality using the GRADE ratings as this would provide a more accurate and meaningful reporting of the evidence for a treatment intervention for women with GDM. Two overview review authors generated the 'Quality assessment tables' using GRADE ratings for *all* other overview review secondary outcomes, not only for the agreed pre-specified GRADE outcomes, as stated in the protocol.

Outcomes

For clarity, one outcome was renamed, and one was removed:

1. Mode of birth (caesarean section) under primary outcomes (maternal) is now listed as caesarean section for clarity, as this is the outcome the overview authors agreed on as an important outcome for women with GDM.

2. Development of type 1 diabetes for maternal long-term outcomes was removed, as this is an unlikely outcome to occur.

Chapter 3: Synthesising the current evidence from randomised controlled trials of different treatment targets for glycaemic control for women with gestational diabetes mellitus

3.1 Preface

This chapter presents a Cochrane systematic review published in the Cochrane Library entitled **'Different intensities of glycaemic control for women with gestational diabetes mellitus'.** The chapter comprises the completed Cochrane systematic review, prepared following production of the review protocol that was peer reviewed and published in the Cochrane Library (Crawford 2015a). The systematic review assessed the available evidence from randomised controlled trials on the effect of different intensities of glycaemic control in pregnant women with GDM on maternal and infant health outcomes.

The chapter aims to address Research Question 2 'Which glycaemic treatment targets best benefit the health of women diagnosed with GDM and their babies'.

The chapter contains the unaltered manuscript accepted for publication. The abstract and key words were removed as directed by the University of Auckland (2016) *Guide to thesis and dissertations*. The 'Plain Language Summary' from the published manuscript is presented at the end of the chapter.

3.2 Different intensities of glycaemic control for women with gestational diabetes mellitus (Review)

3.2.1 Background

Description of the condition

Gestational diabetes mellitus (GDM) is a carbohydrate intolerance resulting in hyperglycaemia, or any degree of glucose intolerance with onset or first recognition during pregnancy from 24 weeks' gestation onwards and which resolves following the birth of the baby (WHO 2013; NICE 2015). The global prevalence of GDM is reported to be between 1% to 25.5%, depending on the diagnostic criteria used and women's ethnicity (ACOG 2013; Bottalico 2007; Cheung 2003; Ferrara 2007; NICE 2015; Sacks 2012), and rates are likely to increase with the reported global obesity epidemic (Athukorala 2010; Kim 2010; Rowlands 2010; Zhang 2010). Obesity has been identified as a significant risk factor for GDM (Boney 2005; Chu 2007; Mokdad 2003; Oteng-Ntim 2012; Rosenberg 2005; Torloni 2009).

During pregnancy, hormones released by the placenta cause an increase in maternal insulin resistance to ensure a constant supply of glucose and other nutrients to the growing fetus (McCance 2011; Wilcox 2005). The maternal pancreas compensates for the pregnancy-induced insulin resistance by secreting more insulin. GDM occurs when this compensatory mechanism fails and not enough insulin is available to metabolise glucose (McCurdy 2010; Wilcox 2005). The maternal blood glucose concentration then increases resulting in hyperglycaemia. Increased amounts of glucose cross the placenta, over-nourishing the fetus, with increased fetal insulin secretion in response (Evans 2009; Ragnarsdottir 2010; Suman Rao 2013). Increased fetal insulin may act as a growth stimulating factor (Pedersen 1954).

Recognised risk factors for developing GDM include obesity, advanced maternal age, weight gain in pregnancy, and a family history of type 2 diabetes (Athukorala 2010; Chu 2007; Kim 2010; Torloni 2009; Zhang 2010). Women of certain ethnicities, such as Asian, African American, Native American, Hispanic, and Pacific Island have an increased risk (Carolan 2012a; Chamberlain 2013; Kim 2013; Schneider 2012).

GDM has major short- and long-term implications for both the mother and her baby. Women with GDM are at higher risk of developing gestational hypertension and pre-eclampsia, and are at increased risk of having a caesarean section (Crowther 2005; HAPO 2008; McCance 2011; NICE 2015). In the long-term, these women are at significantly increased risk of developing cardiovascular disease and over half

will develop type 2 diabetes within five to 10 years (Bellamy 2009). Infants of women with GDM have a greater incidence of being born large-for-gestational age and macrosomic (variously defined as birthweight greater than 4000 g to 4500 g) (Young 2013), which increases the risk of shoulder dystocia and associated birth trauma such as bone fractures and nerve palsy (Athukorala 2006). Macrosomia has been associated with developmental delay in childhood (Ornoy 2005; Slining 2010). In the neonatal period, these infants are at higher risk of hypoglycaemia due to fetal hyperinsulinaemia and need to adjust to not having the high maternal glucose supply (Devlieger 2008). Neonatal hypoglycaemia is associated with developmental delay in childhood (Lucas 1988). There are life-long health risks to the infants of mothers with GDM such as higher rates of obesity and type 2 diabetes in childhood (Page 2014), and an increased risk of diabetes, hypertension, cardiovascular disease in later life (Ornoy 2011), and evidence from published cohort studies indicating an increased risk of postpartum depression (Kozhimannil 2009; Nicklas 2013). Observational neurodevelopmental studies of children of mothers with diabetes (including women with GDM), report a higher rate of neurosensory disability (including gross and fine motor abnormalities, attention deficit hyperactivity disorder (ADHD), learning difficulties, and possibly autism spectrum disorder (ASD)) (Gardener 2009; Krakowiak 2012; Nomura 2012; Ornoy 2015).

Screening and diagnosis of GDM remain controversial, with some countries recommending universal screening of all pregnant women between 24 to 28 weeks' gestation (Nankervis 2013), and others only recommending selective screening (NICE 2015). The amount of glucose recommended for the diagnostic oral glucose tolerance test (OGTT) differs between countries (75 g and 100 g) and there is significant variation in the fasting, one-, two- and three-hour postprandial plasma glucose concentrations above which GDM is diagnosed (ACOG 2013; Nankervis 2013; Ministry of Health 2014; NICE 2015; SIGN 2014; Thompson 2013; WHO 2013).

Similarly, there is wide variation internationally in glycaemic treatment targets recommended for optimal outcomes for women with GDM and their babies (Table 3.1). As evidence emerges that current target thresholds may need to be lower than previously thought to reduce morbidity (Hernandez 2011; Hernandez 2015; Metzger 2008), professional organisations are increasingly advocating lower treatment targets that are closer to observed blood glucose concentrations in pregnant women without GDM (HSE 2010; Nankervis 2013). However, concerns have been raised that lower glycaemic targets may be associated with an increased risk of infants being born small-for-gestational age (Garner 1997;

Langer 1989; Langer 1994), and a potential increased risk of hypoglycaemia in the mother (DCCT 1996), and therefore in, the fetus.

Table 3.1: GDM treatment targets for glycaemic control from clinical practice guidelines

	FPG mmol/L (mg/dL) *	1-hour postprandial mmol/L (mg/dL) *	2-hours postprandial mmol/L (mg/dL) *
Australasian Diabetes in Pregnancy Society (ADIPS) Nankervis 2013 (p.5); 2014 (p. 6) and New Zealand Ministry of Health (Ministry of Health) 2014 (p. 32)	≤ 5.0 (90)	≤ 7.4 (133)	≤ 6.7 (120)
American Diabetes Association (ADA) ADA 2013 (S21) Canadian Diabetes Association (CDA) Thompson 2013 (S178)	≤ 5.3 (95)	≤ 7.8 (140)	≤ 6.7 (120)
National Institute of Health and Clinical Excellence (NICE) NICE 2015 (p. 21)	< 5.3 (95)	< 7.8 (140)	< 6.4 (115)
5th International Workshop on GDM Metzger 2007 (S254)	5.0 (90) to 5.5 (99)	< 7.8 (140)	< 6.7 (120) to 7.1 (127)
Scottish Intercollegiate Guidelines Network SIGN 2014 (p. 59)	4.0 (72) to 6.0 (108)	< 8.0 (144)	< 7.0 (126)
German Diabetes Asociation (DDA) Kleinwechter 2014 (p. 404)	3.6 (65) to 5.3 (95)	< 7.8 (140)	< 6.7 (120)

*RM converted all published glycaemic values for GDM treatment into both mmol/L or mg/dL

Description of the intervention

Treatment of GDM aims to reduce the associated risks of gestational diabetes for the mother and baby by controlling the high maternal blood glucose concentrations (Alwan 2009). Glycaemic control is usually measured by monitoring capillary blood glucose concentrations to ensure blood glucose concentrations are maintained within a pre-defined threshold (Metzger 2008). This may be achieved through the use of diet and lifestyle modifications (ADA 2001; Ministry of Health 2014; NICE 2015; SIGN 2014), or with the addition, if necessary, of pharmacological interventions such as oral hypoglycaemic medications or subcutaneous insulin (ACOG 2013; Ministry of Health 2014; NICE 2015; SIGN 2014). Trials of interventions for GDM usually compare different treatment strategies with glycaemic control as an outcome, not an intervention (Middleton 2012). The focus of this review is comparing different treatment targets of glycaemic control in women with GDM and the impact on maternal and fetal health.

How the intervention might work

There is a continuous relationship between increasing maternal blood glucose concentrations and detrimental maternal and fetal outcomes (Langer 1994; Metzger 2008). Treatment of GDM aims to maintain maternal blood glucose concentrations within certain glycaemic target thresholds, reducing the physiological response of the fetus to elevated maternal blood glucose concentrations and has been shown to be beneficial in reducing perinatal morbidity (Crowther 2005; Landon 2009). The Maternal-Fetal Medicine Units Network (MFMU) trial (Landon 2009) and the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) trial (Crowther 2005), both compared treatment of GDM with no treatment. The MFMU Network trial had tighter glycaemic control targets (fasting plasma glucose < 5.3 mmol/L (95 mg/dL) and two-hour postprandial < 6.7 mmol/L (120 mg/dL)) than the ACHOIS trial (fasting plasma glucose < 5.5 mmol/L (99 mg/dL) and two-hour postprandial < 7.0 mmol/L (126 mg/dL)), and demonstrated a reduction in the risk of caesarean section (risk ratio (RR) 0.79, 97% confidence interval (CI) 0.64 to 0.99) not shown in the ACHOIS trial (RR 0.97, 95% CI 0.81 to 1.16), although both trials demonstrated reductions in birthweight and large-for-gestational-age infants in women with GDM who received treatment compared with women who were not treated (Crowther 2005; Landon 2009; Ornoy 2015). Such evidence suggests lower glycaemic targets may be of benefit.

Why it is important to do this review

The evidence for optimal glycaemic targets for women with GDM is limited and of varying quality (Hernandez 2015). It appears that women who have better controlled blood glucose concentrations in pregnancy have a lower incidence of pre-eclampsia and large-for-gestational-age babies (Crowther 2005; Landon 2009). The infants of these women have a reduced incidence of neonatal hypoglycaemia and perinatal mortality (Landon 2009). Target recommendations from international professional organisations for maternal glycaemic control vary widely, all relying on consensus as there is a lack of high quality evidence (ADA 2013; Metzger 2007; Nankervis 2013; Ministry of Health 2014; NICE 2015; SIGN 2014; Thompson 2013).

In assessing evidence related to determining the optimal degree of glycaemic targets, this review will contribute to knowledge that can be used to minimise the risk of adverse birth outcomes and diabetic complications for pregnant women and their babies.

3.2.2 Objectives

The purpose of this review is to assess the effect of different intensities of glycaemic control in pregnant women with GDM on maternal and infant health outcomes.

3.2.3 Methods

Criteria for considering studies for this review

Types of studies

All published and unpublished randomised controlled trials, cluster-randomised and quasi-randomised controlled trials, including conference abstracts assessing different intensities of glycaemic control for women with GDM, were eligible for inclusion (Higgins 2011). Cross-over trials were not eligible for inclusion, as changes in insulin sensitivity throughout pregnancy make cross-over trials an inappropriate methodology for this review and women with GDM are usually advised of only one glycaemic target range to guide their treatment in their pregnancy.

Types of participants

All pregnant women diagnosed with GDM. Due to varying diagnostic methods and criteria used internationally, we defined screening and subsequent diagnosis and diagnostic criteria as identified in the individual trials. Women with known pre-existing type 1 or type 2 diabetes were excluded.

Types of interventions

The type of intervention includes any glycaemic treatment targets (blood glucose concentration) used for glycaemic control for women with GDM to guide treatment. For further clarity, we converted blood glucose values into both mmol/L and mg/dL as different countries express glucose values in either mmol/L or mg/dL. For example, most Europe, New Zealand, Australia and North America generally use mmol/L and America, China and Germany generally use mg/dL. Trials often express their interventions additionally in non-numerical terms for example: ‘loose’, 'standard care', 'low(er)', 'less tight', ‘moderate’, ‘tight’, ‘very tight’, 'strict(er)', 'intensive therapy' and 'liberal'. We will use the trial definitions to assist with clarity when discussing the results instead of using the numerical ranges repeatedly.

Types of outcome measures

The primary and secondary maternal and infant outcome measures are based on consensus between the review authors and all other review authors of Cochrane systematic reviews for treatment of GDM.

Primary outcomes

Maternal

1. Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia).
2. Subsequent development of type 2 diabetes.

Infant

1. Perinatal (fetal and neonatal) mortality.
2. Large-for-gestational age (birthweight greater than the 90th centile; or as defined by individual trial).
3. Composite of mortality or serious morbidity (variously defined by trials, e.g. infant death, shoulder dystocia, bone fracture or nerve palsy).
4. Neurosensory disability (variously defined by individual trials).

Secondary outcomes

Maternal

1. Caesarean section.
2. Maternal mortality.
3. Weight gain during pregnancy.
4. Placental abruption.
5. Induction of labour.
6. Perineal trauma.
7. Postpartum haemorrhage.
8. Postpartum infection requiring use of antibiotics (variously defined).
9. Maternal hypoglycaemia.
10. Glycaemic control during/end of intervention (as defined by trialists).
11. Use of pharmacological treatment (insulin, oral hypoglycaemics).
12. Relevant biomarker changes associated with the intervention (including adiponectin, free fatty acids, triglycerides, high density lipoproteins, low density lipoproteins, insulin).
13. Breastfeeding.
14. Adherence with treatment/management.
15. Sense of wellbeing and quality of life.

16. Views of the intervention.
17. Behaviour change associated with the intervention.

Long-term maternal outcomes

1. Postnatal depression.
2. Postnatal weight retention or return to pre-pregnancy weight.
3. Body mass index (BMI).
4. GDM in a subsequent pregnancy.
5. Type 1 diabetes mellitus.
6. Impaired glucose tolerance.
7. Cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome).

Infant

1. Stillbirth.
2. Neonatal death.
3. Macrosomia (birthweight ≥ 4000 g, or as defined by individual trial).
4. Small-for-gestational age (birthweight less than the 10th centile, or as defined by individual trial).
5. Shoulder dystocia.
6. Bone fracture.
7. Nerve palsy.
8. Preterm birth (< 37 weeks' gestation; < 32 weeks' gestation).
9. Gestational age at birth.
10. Birthweight and z score.
11. Head circumference and z score.
12. Length and z score.
13. Ponderal index.
14. Hypoglycaemia (variously defined).
15. Respiratory distress syndrome.
16. Neonatal jaundice (hyperbilirubinaemia).
17. Hypocalcaemia.
18. Adiposity (variously defined by trials, e.g. skinfold thickness, fat mass).

19. Polycythaemia.
20. Apgar score < seven at five minutes.
21. Relevant biomarker changes associated with the intervention (including cord c peptide, cord insulin).

Later childhood

1. Weight and z score.
2. Height and z score.
3. Head circumference and z score.
4. Adiposity (including BMI, skinfold thickness).
5. Blood pressure.
6. Type 1 diabetes mellitus.
7. Type 2 diabetes mellitus.
8. Impaired glucose tolerance.
9. Dyslipidaemia or metabolic syndrome.
10. Educational achievement.

Adulthood outcomes

1. Weight.
2. Height.
3. Adiposity (including BMI, skinfold thickness, fat mass).
4. Cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome).
5. Type 1 diabetes mellitus.
6. Type 2 diabetes mellitus.
7. Impaired glucose tolerance.
8. Dyslipidaemia or metabolic syndrome.
9. Employment, education, and social status/achievement.

Health services

1. Number of antenatal visits or admissions.

2. Number of hospital or health professional visits (including midwife, obstetrician, physician, dietician, diabetic nurse).
3. Admission to neonatal intensive care unit/nursery.
4. Length of antenatal stay.
5. Length of postnatal stay (maternal).
6. Length of postnatal stay (baby).
7. Cost of maternal care.
8. Cost of offspring care.
9. Costs associated with the intervention.
10. Costs to families associated with the management provided.

Search methods for identification of studies

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (31 January 2016). The Register is a database containing over 20,000 reports of controlled trials in the field of pregnancy and childbirth. For full search methods used to populate the Pregnancy and Childbirth Group's Trials Register including the detailed search strategies for CENTRAL, MEDLINE, Embase and CINAHL; the list of hand-searched journals and conference proceedings, and the list of journals reviewed via the current awareness service, please follow this link to the editorial information about the Cochrane Pregnancy and Childbirth Group in *The Cochrane Library* and select the '***Specialized Register*** ' section from the options on the left side of the screen. Briefly, the Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

- monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
- weekly searches of MEDLINE (Ovid); weekly searches of Embase (Ovid); monthly searches of CINAHL (EBSCO);
- hand-searches of 30 journals and the proceedings of major conferences;
- weekly current awareness alerts for a further 44 journals

- monthly BioMed Central email alerts.

Search results are screened by two people and the full text of all relevant trial reports identified through the searching activities described above is reviewed. Based on the intervention described, each trial report is assigned a number that corresponds to a specific Pregnancy and Childbirth Group review topic (or topics) and is then added to the Register. The Trials Search Co-ordinator searches the Register for each review using this topic number rather than keywords. This results in a more specific search set which has been fully accounted for in the relevant review sections (Included, Excluded, Awaiting Classification or Ongoing studies).

In addition, we searched ClinicalTrials.gov, and the WHO International Clinical Trials Registry Platform (ICTRP) (1 February 2016) for unpublished, planned and ongoing trial reports using the following search terms:

- glycemic control AND pregnancy
- glycemic control AND pregnant
- glycaemic control AND pregnancy
- glycaemic control AND pregnant
- glycaemic control AND gestational
- glycemic control AND gestational
- gestational diabetes mellitus AND treatment thresholds
- gestational diabetes mellitus AND treatment targets

Searching other resources

We searched reference lists of retrieved studies. We did not apply any language or date restrictions.

Data collection and analysis

The following methods were used for assessing the eight reports that were identified as a result of the search and is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Selection of studies

Two review authors independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We had no disagreement, hence did not require to consult with a third author.

We created a Study flow diagram to map out the number of included and excluded records identified (Figure 3.1).

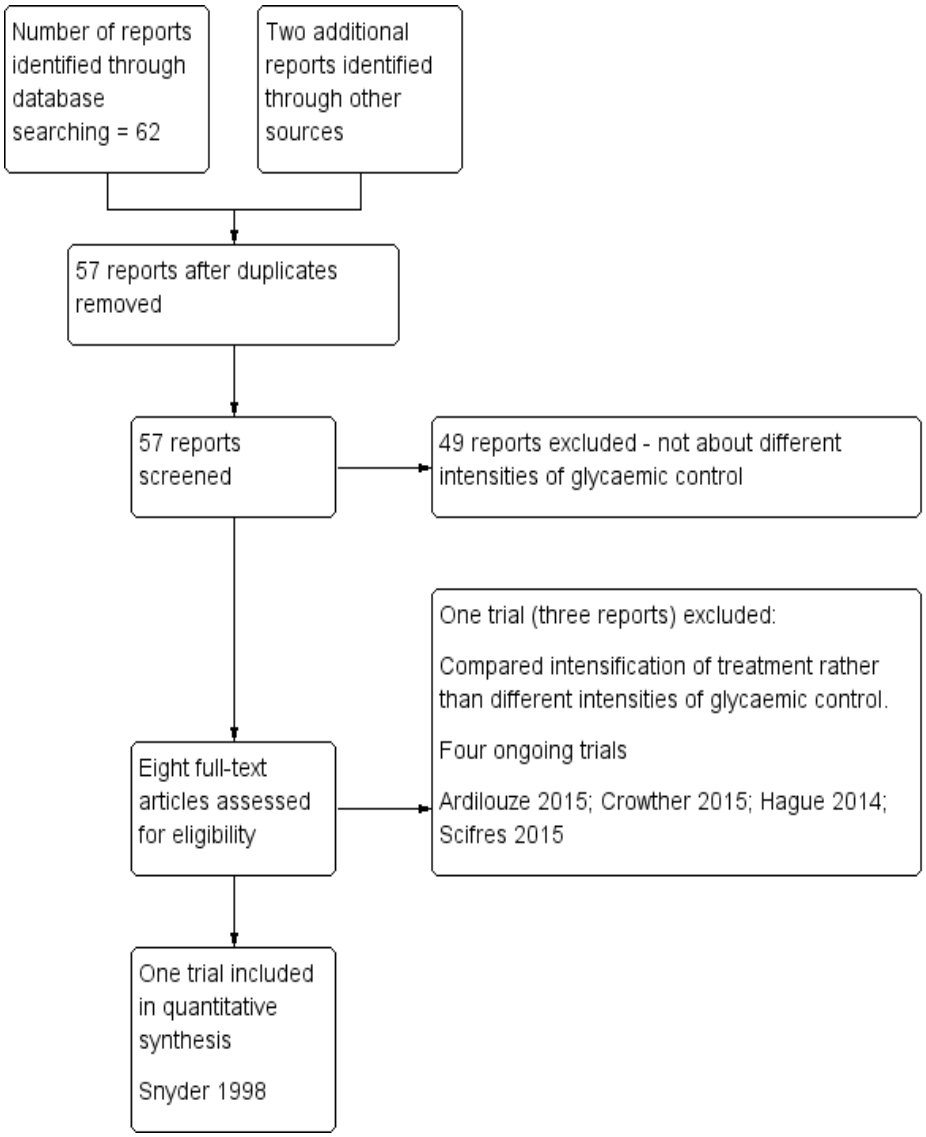
Data extraction and management

We used the Cochrane Pregnancy and Childbirth Group data extraction form. Two review authors (RM and JB) extracted data from the one identified study using the agreed form. We entered the data into Review Manager software (RevMan 2014) and checked for accuracy.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias for the one included study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved any disagreement by discussion or by involving a third author. Seeking statistical advice for calculating intra cluster correlations from cluster-randomised trials as outlined in our published protocol, was not required.

Figure 3.1: Study flow diagram



(1) Random sequence generation (checking for possible selection bias)

We described for the 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 assessed the method as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We described for the included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We assessed the methods as:

- low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We described for the included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies are at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described for the included study the methods used, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed methods used to blind outcome assessment as:

- low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

We described for the included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported, and 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. We attempted to contact the trial authors for further information and planned to include any relevant missing data in the analyses which we undertook.

We assessed methods as:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation);
- unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We described for the included study how we investigated the possibility of selective outcome reporting bias and what we found.

We assessed the methods as:

- low risk of bias (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);
- high risk of bias (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 risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

We described for the included study any important concerns we have about other possible sources of bias. We assessed whether the study was free of other problems that could put it at risk of bias:

- low risk of other bias;
- high risk of other bias;
- unclear whether there is risk of other bias.

Overall risk of bias

We made explicit judgements about whether the study was at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether it impacted on the findings. We explored the impact of the level of bias through undertaking sensitivity analyses - see sensitivity analysis (page 353).

Assessment of the quality of the evidence using the GRADE approach

We assessed the quality of the evidence of the included trial using the GRADE approach as outlined in the GRADE Handbook Chapter 5 (Schünemann 2013) with the software GRADEpro GDT (GRADEpro GDT 2015) producing two 'Summary of findings' tables. A summary of the intervention effect and a measure of quality for each of the following outcomes was produced using the GRADE approach. GRADEpro five criteria (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of the body of evidence for each outcome. We chose seven maternal and seven child (as neonate, child, adult) outcomes (seven are the maximum of outcomes permitted with this software), as listed below. These are based on consensus between the review authors and all other review authors of Cochrane systematic reviews for treatment of GDM. For the included trial the only outcome (maternal) able to be assessed for quality was caesarean section, no other data were available for the other listed outcomes.

Maternal

1. Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia).
2. Caesarean section.
3. Subsequent development of type 2 diabetes.

4. Perineal trauma.
5. Return to pre-pregnancy weight.
6. Postnatal depression.
7. Induction of labour.

Child (as neonate, child, adult)

1. Large-for-gestational age.
2. Perinatal mortality.
3. Composite of mortality and serious morbidity.
4. Neonatal hypoglycaemia.
5. Adiposity.
6. Diabetes.
7. Neurosensory disability.

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratio (RR) with 95% confidence intervals (CI).

Continuous data

For continuous data, we used the mean difference (MD). In future updates, if appropriate, we will use the standardised mean difference (SMD) to combine trials that measure the same outcome, but use different methods.

Unit of analysis issues

Cluster-randomised trials

No cluster-randomised trials were identified. If cluster-randomised trials are identified in future updates of this review we will make adjustments to the standard errors using the methods described in the *Handbook* [Section 16.3.6] using an estimate of the intra cluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in

the ICC. We will consider it reasonable to combine the results from both cluster-randomised trials and individually-randomised trials 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.

Multiple pregnancy

The included trial did not report on multiple pregnancy. If in the future updates of this review, trials do report on multiple pregnancy, we will present maternal data as per woman randomised and neonatal data per infant.

Multiple-arm studies

The included trial is this review was not a multiple arm trial. In future updates of the review, where a trial has multiple intervention arms, we will avoid 'double counting' of participants by combining groups to create a single pair-wise comparison if possible. Where this is not possible, we will split the 'shared' group into two or more groups with smaller sample size and include two or more (reasonably independent) comparisons.

Dealing with missing data

For the included study, we noted the levels of attrition did not exceed 20%. In future updates of the review, we will explore the impact of including studies with high levels of missing data (> 20%) in the overall assessment of treatment effect by using sensitivity analysis.

For all outcomes, we carried out analyses, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses, and all participants were 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 is the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

We planned to assess statistical heterogeneity in each meta-analysis using the Tau^2, I^2 and Chi^2 statistics, but identified only one trial. If future updates include further trials then we will regard heterogeneity as substantial if an I^2 is greater than 30% and either a Tau^2 is greater than zero, or there is a low P value (less than 0.10) in the Chi^2 test for heterogeneity (Higgins 2011).

Assessment of reporting biases

A single trial is included in this review. In future updates, 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. If asymmetry is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2014). Only one trial was included so there are no data combined in meta-analysis. In future updates, 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. In future updates, if more trials are included and there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials is considered clinically meaningful. The random-effects summary will be treated as the average of the 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, the results will be presented as the average treatment effect with 95% confidence intervals, and the estimates of Tau^2 and I^2.

Subgroup analysis and investigation of heterogeneity

As there is currently only a single trial included in the review, we have not explored heterogeneity or subgroup analyses. If, in future updates, 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 a random-effects model.

We will not combine trials based on the individual trial definition of intensity of glycaemic control. We will use the mmol/L(mg/dL) thresholds used in the trials and subgroups based on these if there is significant heterogeneity.

1. Types of strategies used to target or achieve glycaemic control, or both

i) Diet and lifestyle changes alone versus

ii) Oral hypoglycaemics +\- diet and lifestyle changes versus

iii) Insulin therapy +\- diet and lifestyle changes.

2. Criteria used for diagnosis of GDM

i) International Association of Diabetes in Pregnancy Study Group (IADPSG 2010), Australasian Diabetes in Pregnancy Society (Nankervis 2013); World Health Organization (WHO 2013); American Diabetes Association (ADA 2013); Scottish Intercollegiate Guidelines Network (SIGN 2014) versus

ii) New Zealand Ministry of Health (Ministry of Health 2014) versus

iii) National Institute of Health and Clinical Excellence (NICE 2015) versus

iv) Canadian Diabetes Association (Thompson 2013) versus

v) American College of Obstetricians and Gynecologists (ACOG 2013) versus

vi) Carpenter et al (Carpenter 1982) versus

vii) National Diabetes Data Group (National Data Group 1979) versus

viii) Hoffmann et al (ADIPS) (Hoffman 1998), NICE (NICE 2008), WHO (WHO 1999) versus

ix) Any others identified by individual trial.

3. Gestational age at diagnosis

i) < 24 weeks versus

ii) 24 to < 28 weeks versus

iii) ≥ 28 weeks.

4. Woman's ethnicity as identified from the trials

5. Women who are primiparas versus multiparas

6. Twin pregnancies versus singleton pregnancies

The following outcomes would be used in any subgroup analyses:

Maternal

1. Hypertensive disorders of pregnancy.
2. Subsequent development of type 2 diabetes.

Infant

1. Perinatal (fetal and neonatal) mortality.
2. Large-for-gestational age (birthweight greater than the 90th centile; or as defined by individual trial).
3. Composite of mortality or serious morbidity.

In future updates if further trials are identified for inclusion, we will assess subgroup differences by interaction tests available within RevMan (RevMan 2014) and report the results of subgroup analyses quoting the Chi² statistic and P value, and the interaction test I² value.

Sensitivity analysis

Planned sensitivity analyses were not needed. In future updates will carry out sensitivity analysis, if required, to investigate the effect of the randomisation unit where we include cluster-randomised trials along with individually-randomised trials. We will also carry out sensitivity analysis to explore the impact of including studies assessed as high risk of bias due to randomisation method (e.g. quasi-randomisation versus true randomisation), and allocation concealment on the primary outcomes in order to assess whether this makes any difference to the overall results. In addition, we will perform sensitivity analysis by excluding trials assessed as high risk of bias due to missing data.

3.2.4 Results

Description of studies

Results of the search

We identified eight reports of six trials. Two trials (Garner 1997; Snyder 1998) are published (four reports) (Figure 3.1) and four (Ardilouze 2015; Crowther 2015; Hague 2014; Scifres 2015) are ongoing studies (Table 3.2).

Table 3.2: Characteristics of ongoing studies

Author and year (Study ID)	Ardilouze 2015
Study name	Glycemic objectives of women with GDM.
Methods	Randomised controlled trial. Unblinded. Canada.
Participants	30 women, 15-32 weeks' gestation. Excluded: known type 1 or type 2 diabetes, treatment interfering with glucose metabolism.
Interventions	*Normal* glycaemic control target: fasting: 5.3 mmol/L (95 mg/dL) and 2-hour after meals: 6.7 mmol/L (120 mg/dL). Using diet, physical exercise, or insulin to reach normal glycaemic control. *Low* glycaemic control target: fasting: 4.8 mmol/L (86 mg/dL) and 2-hour after meals: 5.9 mmol/L (106 mg/dL). Using diet, physical exercise, or insulin to reach low glycaemic control.
Outcomes	Primary outcome: fetal glycated haemoglobin at delivery. Secondary outcome: treatment satisfaction.
Starting date	March 2015.
Contact information	Jean-Luc Ardilouze: Jean-Luc.Ardilouze@USherbrooke.ca Julie Menard: jumenard.chus@ssss.gouv.qc.ca
Notes	Clinical Trial Identifier: NCT02478762.

Author and year (Study ID)	Crowther 2015
Study name	Optimal glycaemic targets for women with gestational diabetes: the randomised trial - TARGET.
Methods	Multi-centre, stepped wedge, cluster-randomised controlled trial. Funding: Health Research Council of New Zealand.
Participants	A total sample size of 1080 participant from 10 hospitals in New Zealand providing care for women newly diagnosed with GDM. Inclusion criteria: pregnant women newly diagnosed with GDM between 24-34 weeks' gestation and receiving treatment for GDM. Exclusion criteria: pregnant women with GDM where the fetus has a major anomaly.
Interventions	*Less tight* glycaemic targets for glycaemic control in women newly diagnosed with GDM - fasting plasma glucose < 5.5 mmol/L (99 mg/dL); 1-hour postprandial < 8.0 mmol/L (144 mg/dL); 2-hour postprandial < 7.0 mmol/L (126 mg/dL). These targets will be used by the responsible clinician for glycaemic control following diagnosis of GDM until the birth of the baby until stepped wedged cluster-randomisation occurs for the intervention to:

Author and year (Study ID)	Crowther 2015
	tight glycaemic targets for glycaemic control in women newly diagnosed with GDM fasting plasma glucose ≤ 5.0 mmol/L (90 mg/dL); 1-hour postprandial ≤ 7.4 mmol/L 133mg/dL); 2-hour postprandial ≤ 6.7 mmol/L (120 mg/dL). These targets will be used by the responsible clinician for glycaemic control following diagnosis of GDM until the birth of the baby.
Outcomes	Primary outcome: large-for-gestational-age infant (birthweight >90th centile using customised charts). Secondary outcomes: up to the time of hospital discharge after birth: **for the woman:** pre-eclampsia, induction of labour, mode of birth, gestational weight gain, maternal hypoglycaemia, mean daily fasting and postprandial capillary glucose concentration during treatment, proportion of glucose values within target, diet quality, physical activity, length of postnatal stay, health status, anxiety, depression and breastfeeding at discharge, resource utilisation. **for the baby:** perinatal death, birth trauma, nerve palsy, bone fracture, shoulder dystocia; gestational age at birth, birthweight, macrosomia, small-for-gestational age, length, head circumference, fat mass, respiratory support, hypoglycaemia, hyperbilirubinaemia, lipid and inflammatory markers from cord blood, neonatal intensive care unit admission, length of postnatal stay, resource utilisation.
Starting date	29.05.2015.
Contact information	Professor Caroline Crowther, The Liggins Institute, The University of Auckland 85 Park Road, Grafton, Auckland 1023, New Zealand. Ph.+64 9 923 6011; c.crowther@auckland.ac.nz
Notes	Clinical Trial Identifier: ACTRN12615000282583.

Author and year (Study ID)	Hague 2014
Study name	An evaluation of the safety of very tight glycaemic control versus tight glycaemic control in women with gestational diabetes - GluT pilot.
Methods	Randomised controlled trial. Funding: Women's and Children's Hospital, Adelaide, SA, Australia; Robinson Research Institute University of Adelaide, SA, Australia; Novo Nordisk Regional Support Scheme for 2013, Baulkham Hills, NSW, Australia.
Participants	40 women with GDM diagnosed on 75 g OGTT: fasting glucose ≥ 5.5 mmol/L (99 mg/dL) and 2 hours glucose ≥ 8.5 mmol/L (153 mg/dL), between 12 and 30 weeks' gestation, with a singleton or twin pregnancy, not previously diagnosed as diabetic, attending antenatal care at collaborating hospitals, and giving informed written consent. Minimum age 18 years. Exclusion criteria > 30 + 0 weeks' gestation, or with triplets or higher order gravidity, or with major active medical disorders (including psychiatric disease requiring antipsychotic medication and inflammatory disorders requiring corticosteroid therapy, but not including chronic hypertension).
Interventions	*Very tight* glycaemic control as monitored by self-monitoring of blood glucose with a memory glucometer, aiming to keep fasting capillary blood glucose < 5.0 mmol/L (90 mg/dL) and 2-hour postprandial capillary blood glucose < 6.7 mmol/L (120 mg/dL) until birth, using diet, exercise, insulin, other drugs, as necessary, and at appropriate doses to maintain the control, under the supervision of an obstetric physician and a diabetes nurse

Author and year (Study ID)	Hague 2014
	educator and *tight* glycaemic* control as monitored by self-monitoring blood glucose with a memory glucometer, aiming to keep fasting capillary blood glucose < 5.5 mmol/L (99 mg/dL) and 2-hour postprandial < 7.0 mmol/L (126 mg/dL) until birth, using diet, exercise, insulin, other drugs, as necessary, and at appropriate doses to maintain the control, under the supervision of an obstetric physician and a diabetes nurse educator. *email correspondence confirmed the tight glycaemic targets as stated above. On the ANZCTR very tight and tight glycaemic targets are listed as the same glycaemic targets, which according to Hague is a typo and will be rectified soon. At time of submission of this review it had not been corrected.
Outcomes	Primary outcomes: maternal hypoglycaemia: self-monitoring capillary blood glucose < 3.0 mmol/L (54 mg/dL) - number of episodes, symptomatic or not and severe maternal hypoglycaemia: self-monitoring capillary blood glucose < 2.5 mmol/L (45 mg/dL) - number of episodes. Secondary outcomes: birthweight; neonatal hypoglycaemia in whole blood from heel prick < 2.6 mmol/L (47 mg/dL); severe neonatal hypoglycaemia in whole blood from heel prick < 2.0 mmol/L (36 mg/dL).
Starting date	23.12.2014.
Contact information	Professor William "Bill" Hague, Women's and Children's Hospital, 72 King William Road, North Adelaide, SA 5006, Australia, Ph. +61 4 11114575; bill.hague@adelaide.edu.au
Notes	Clinical Trial Identifier: ACTRN12614001250628.

Author and year (Study ID)	Scifres 2015
Study name	Randomised controlled clinical pilot trial of intensive management for gestational diabetes (GDM-MOMS).
Methods	Randomised clinical pilot trial designed to assess the feasibility of randomising obese women with GDM to lower glycaemic thresholds compared to standard care. Neither patients nor their providers will be blinded to patient study group. All women will receive standard nutritional counselling at the time of diagnosis, and they will also be treated with either glyburide or insulin as dictated by standard care.
Participants	60 obese women with a new diagnosis of GDM using the Carpenter-Coustan criteria, singleton gestation, between 20-30 weeks of gestation.
Interventions	Active comparator "*Standard care*": target fasting blood glucose values < 95 mg/dL (5.3 mmol/L) and 1-hour postprandial values < 140 mg/dL (7.8 mmol/L). Experimental "*Intensive therapy*": target fasting blood glucose values < 90 mg/dL (5.0 mmol/L) and 1-hour postprandial values < 120 mg/dL (6.7 mmol/L).
Outcomes	Primary outcome: change in baseline maternal glycaemia at 32-36 weeks' gestation. Secondary outcomes: neonatal body composition, cytokine measurements, physical activity, sleep assessments, patient questionnaires, lipid measurements, glucose measurements.
Starting date	June 2015 (estimated study completion date: September 2018, estimated primary outcome measure completion date: September 2017).
Contact information	Christina Scifres, MD, University of Oklahoma christy-zornes@ouhsc.edu and stephanie-boothroyd@ouhsc.edu
Notes	Clinical Trial Identifier: NCT02530866.

Included studies

We included one study (Snyder 1998) in this review. The publication, from Canada, was in abstract form only. No full-text publication has been identified. RM emailed co-author (Meltzer) for further information, as Meltzer was the only author with a contact email address found via the Internet. Synder, the main author and co-authors Morin and Nadeau were not contactable. No response from Meltzer was received at time of submission.

Snyder 1998, was conducted in Canada and involved 180 women. The women were diagnosed with GDM between 20 to 32 weeks' gestation and were recruited over a 12-month period (1996 to 1997). The study compared *strict* versus *liberal* glycaemic targets for glycaemic control for women treated with insulin. *Strict* glycaemic targets for insulin treatment were defined as (pre-prandial: 5.0 mmol/L (90 mg/dL) and at one-hour postprandial: 6.7 mmol/L (120 mg/dL)) and *liberal* glycaemic targets were defined as (pre-prandial: 5.8 mmol/L (104 mg/dL) and at one-hour postprandial: 7.8 mmol/L (140 mg/dL)). No other inclusion criteria were detailed. Data for other characteristics (pre-pregnancy body mass index (BMI), maternal age, gestational age at diagnosis and length of treatment) and the criteria used to diagnose GDM were not reported. No funding sources were identified (Table 3.3).

Table 3.3: Characteristics of included studies

Author and year (Study ID)	Snyder 1998
Methods	Randomised controlled trial.
Participants	180 women. Inclusion criteria: pregnant women, 20 to 37 weeks' gestation, referred for GDM (no details of diagnostic criteria). Exclusion criteria: no details. Setting: Royal Victoria Hospital, McGill University, Montreal, Canada. Timing: 1996 to 1997.
Interventions	*Liberal* glycaemic control criteria: before meal 5.8 mmol/L (104 mg/dL) and 1-hour postprandial 7.8 mmol/L (140 mg/dL). Monitored weekly and twice a week after 32 weeks'. Birth planned before 40 weeks' gestation (n = 86). Treated with Insulin if outside *liberal* glycaemic targets. *Strict* glycaemic control criteria: before meal 5.0 mmol/L (90 mg/dL) and 1-hour postprandial 6.7 mmol/L (120 mg/dL). Monitored weekly and twice a week after 32 weeks'. Birth planned before 40 weeks' gestation (n = 85). Treated with Insulin if outside *strict* glycaemic targets.
Outcomes	Insulin therapy, caesarean section, gestational age at birth, birthweight, birthweight > 4 kg, small-for-gestational age, induction of labour, neonatal birth trauma, neonatal metabolic disturbances.
Notes	Sample size calculation - not reported. ITT analysis - not clear, data reported for 171/180 women. Conference abstract only. One of the authors, Sara Meltzer, was contacted via email to request further information, e.g. study protocol or any further unpublished papers. No response was received at time of submission.

Excluded studies

We excluded one study (Garner 1997) as it was a study of intensification of treatment, not of comparing different intensities of glycaemic control targets in women diagnosed with GDM (Table 3.4).

Table 3.4: Characteristics of excluded studies

Author and year (Study ID)	Garner 1997
Reason for exclusion	In this Canadian study, 300 women diagnosed with GDM were randomised to either receive 'intensive' follow-up care or 'routine care'. 'Intensive' follow-up care took place with an obstetrician and an endocrinologist in a tertiary setting and after receiving dietary counselling women were placed on a calorie-restricted diet. Daily blood glucose estimations were obtained, women were seen bi-weekly at the hospital where biophysical profiles were performed at each visit and ultra-sonographic assessments for fetal growth, amniotic fluid volume and cardiac size performed. In the 'routine care' group, women were not seen by a dietician, advised stay on an unrestricted healthy diet, performed only 2 glucose levels weekly at home and returned for follow-up care to their primary obstetric care provider in the community. No high-risk monitoring of the fetus unless there was an indication. All women in the trial were recommended to maintain their fasting glucose level < 4.4 mmol/L (79 mg/dL) and 1-hour postprandial < 7.8 mmol/L (140 mg/dL). The intensification of the treatment was compared between the 2 groups, not different intensities of glycaemic control.

Risk of bias in included studies

The overall quality of the included study was judged to be unclear as it was only published as a conference abstract and provided limited information about the methods used.

The 'Risk of bias' summaries (Table 3.5; Figure 3.2; Figure 3.3) present the review authors' judgements about each 'Risk of bias' item from the included study.

Table 3.5: Risk of bias summary for included study Snyder 1998

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	'Randomised' no other details provided.
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding of participants and personnel (performance bias)	High risk	No details but blinding unlikely.
Blinding of outcome assessment (detection bias)	Unclear risk	No details as to whether outcome assessors were blinded.
Incomplete outcome data (attrition bias)	Unclear risk	Data reported on 171 of 180 women enrolled. No details on loss to follow-up.

Bias	Authors' judgement	Support for judgement
Selective reporting (reporting bias)	High risk	Conference abstract only. Data not reported for all outcomes, only stated that no differences.
Other bias	High risk	Authors state that there was no difference between groups at baseline, but no data provided. No protocol has been identified for this trial and no full publication has been identified.

Figure 3.2: 'Risk of bias' summary: review authors' judgements about each risk of bias item from the included study

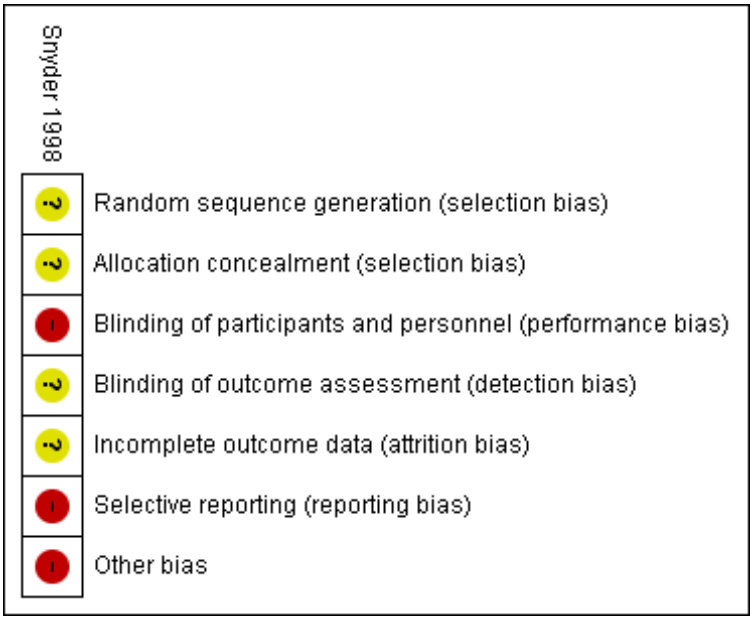
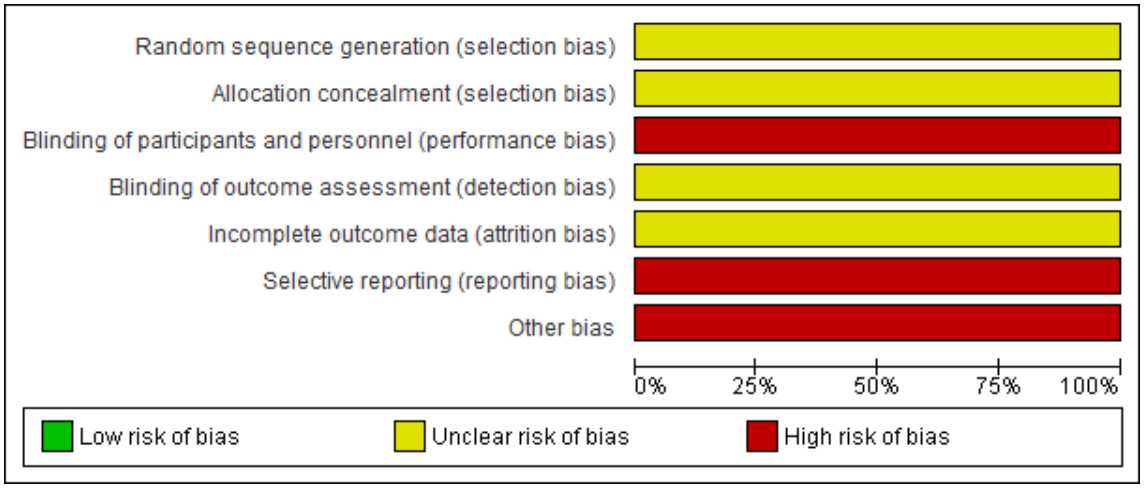


Figure 3.3: 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages from the included study



Allocation (selection bias)

The method of random sequence generation was not described in detail. Allocation concealment was not described.

Blinding (performance bias and detection bias)

In this study the blinding of women, their clinical carers and the researcher to group allocation was most likely not feasible. A lack of blinding may have influenced the study outcomes. No details were provided as whether or not there was blinding of outcome assessors.

Incomplete outcome data (attrition bias)

Data are reported for 171 of 180 women who were recruited to the study (Snyder 1998). No data for the missing nine women were provided. Intention-to-treat analysis is not reported.

Selective reporting (reporting bias)

As the included study was only published in abstract form it is unclear if the data reported represent all of the pre-specified outcomes for the study or if only selected outcomes are reported.

Other potential sources of bias

It was not possible to judge if there were other sources of bias as little information is provided in the conference abstract. The statement "the groups were comparable for pre-pregnancy body mass, maternal age, gestational age at diagnosis and length of treatment" is not substantiated with any data.

Effects of interventions

Summary of findings for the main comparison are presented in the following tables: Intensity of glycaemic control for women with GDM – strict versus liberal glycaemic targets (maternal outcomes) (Table 3.6) and for their children (as neonate, child, adult) (Table 3.7).

Table 3.6: Summary of findings: Intensity of glycaemic control for women with gestational diabetes mellitus - *strict* glycaemic targets versus *liberal* glycaemic targets (Maternal outcomes)

Patient or population: Women with GDM **Setting:** Canada
Intervention: Strict intensity of glycaemic control: pre-prandial: 5.0 mmol/L (90 mg/dL) and at one-hour postprandial: 6.7 mmol/L (120 mg/dL)
Comparison: Less strict glycaemic control: pre-prandial 5.8 mmol/L (104 mg/dL) and at one-hour postprandial 7.8 mmol/L (140 mg/dL)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Evidence Quality (GRADE)*	Comments
	Risk with less strict glycaemic control	Risk with strict glycaemic control				
Hypertensive disorders of pregnancy			not estimable	(0 studies)		No data reported for hypertensive disorders of pregnancy.
Caesarean section	**244 per 1000**	**330 per 1000** (203 to 532)	**RR 1.35** (0.83 to 2.18)	171 (1 study)	⊕⊖⊖⊖ **very low**[1,2,3]	
Subsequent development of type 2 diabetes			not estimable	(0 studies)		No data reported for subsequent development of type 2 diabetes.
Perineal trauma			not estimable	(0 studies)		No data reported for perineal trauma.
Return to pre-pregnancy weight			not estimable	(0 studies)		No data reported for return to pre-pregnancy weight.
Postnatal depression			not estimable	(0 studies)		No data reported for postnatal depression.
Induction of labour (IOL)			not estimable	(0 studies)		No data reported for IOL.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence: High quality: Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.

[1] Lack of detail to make a judgement about random sequence generation, allocation concealment, attrition bias and reporting bias. Open label study. No details regarding blinding of outcome assessors.
[2] Wide confidence intervals that cross the line of no effect. [3] Evidence based on a single trial that was only published in conference abstract form.

Table 3.7: Intensity of glycaemic control for women with gestational diabetes mellitus - strict glycaemic targets versus liberal glycaemic targets (Child (as neonate, child, adult) outcomes)

Patient or population: Children (as neonate, child, adult) of women with GDM **Setting:** Canada
Intervention: Strict intensity of maternal glycaemic control: pre-prandial: 5.0 mmol/L (90 mg/dL) and at one-hour postprandial: 6.7 mmol/L (120 mg/dL)
Comparison: Less strict maternal glycaemic control: pre-prandial 5.8 mmol/L (104 mg/dL) and at one-hour postprandial 7.8 mmol/L (140 mg/dL)

Outcomes	Anticipated absolute effects*(95%CI)		Relative effect (95% CI)	№ of participants (studies)	Evidence Quality (GRADE)*	Comments
	Risk with less strict glycaemic control	Risk with strict glycaemic control				
Large-for-gestational age - not reported	see comment	see comment	not estimable	(0 studies)	-	No data reported for large-for-gestational age in the included study.
Perinatal mortality - not reported	see comment	see comment	not estimable	(0 studies)	-	No data reported for perinatal mortality in the included study.
Composite of mortality and serious morbidity - not reported	see comment	see comment	not estimable	(0 studies)	-	No data reported for composite of mortality and serious morbidity in the included study.
Neonatal hypoglycaemia - not reported	see comment	see comment	not estimable	(0 studies)	-	No data reported for neonatal hypoglycaemia in the included study.
Adiposity - not reported	see comment	see comment	not estimable	(0 studies)	-	No data reported for adiposity in the included study.
Diabetes - not reported	see comment	see comment	not estimable	(0 studies)	-	No data reported for diabetes in the included study.
Neurosensory disability - not reported	see comment	see comment	not estimable	(0 studies)	-	No data reported for neurosensory disability in the included study.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence: High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Primary outcomes

Maternal outcomes

No data were reported for **hypertension disorders of pregnancy** or **subsequent development of type 2 diabetes**.

Infant outcomes

No data were reported for any of the neonatal primary outcomes for this review (**perinatal (fetal and neonatal) mortality**; **large-for-gestational age**; **composite of death or severe morbidity** or later childhood **neurosensory disability**).

Secondary outcomes

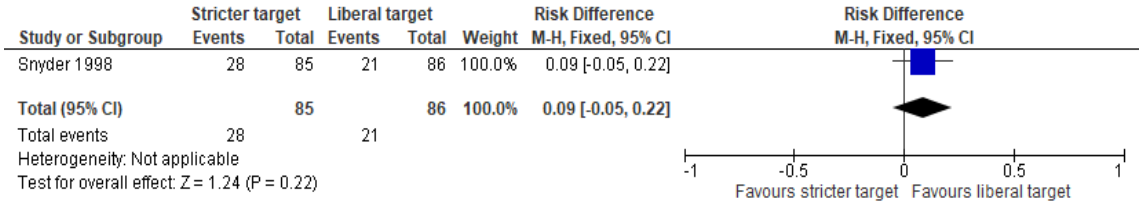
Table 3.8: Comparison 1: Intensity of glycaemic control – strict glycaemic targets versus liberal glycaemic targets

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caesarean section	1	171	Risk Ratio (M-H, Fixed, 95% CI)	1.35 [0.83, 2.18]
2 Use of pharmacological therapy	1	171	Risk Ratio (M-H, Fixed, 95% CI)	1.85 [1.14, 3.03]
3 Macrosomia	1	171	Risk Ratio (M-H, Fixed, 95% CI)	1.35 [0.31, 5.85]
4 Small-for-gestational age	1	171	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.48, 2.63]
5 Gestational age at birth (weeks)	1	171	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-0.73, 0.13]
6 Birthweight	1	171	Mean Difference (IV, Fixed, 95% CI)	-92.0 [-241.97, 57.97]

Maternal outcomes

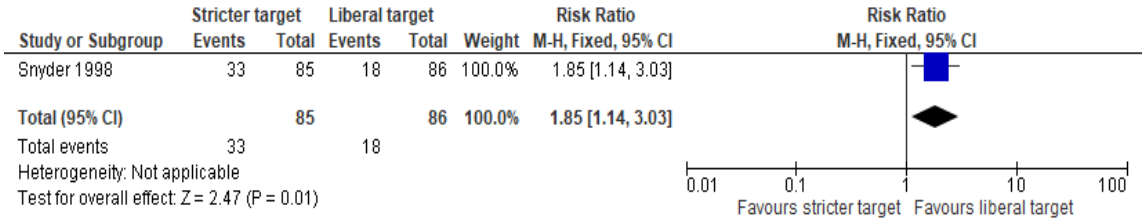
Twenty-eight of 85 (33%) women in the *strict* group had a caesarean section compared with 21 of 86 women (24%) in the *liberal* group. There was no difference in risk of birth by **caesarean section** (risk ratio (RR) 1.35, 95% confidence interval (CI) 0.83 to 2.18, one trial, 171 women), (Table 3.8; Table 3.9). Caesarean section was the only pre-specified outcome with available data for GRADE assessment. The quality of the evidence for caesarean section was judged to be *very low* due to lack of details for the individual components of risk of bias, evidence of imprecision and publication bias. The chance of birth by caesarean section in the *liberal* glycaemic target group was 24%; for women in the *strict* glycaemic control group the chance of birth by caesarean section ranged from 20% to 53%.

Table 3.9: Analysis comparison I: Intensity of glycaemic control - strict glycaemic targets versus liberal glycaemic targets. Outcome 1: Caesarean section



Strict glycaemic targets were associated with an increase in the **use of pharmacological therapy** (identified as the use of insulin in this study) (33/85; 39%) compared with *liberal* glycaemic targets (18/86; 21%) (RR 1.85, 95% CI 1.14 to 3.03; one trial, 171 women), (Table 3.8; Table 3.10). CIs are wide suggesting imprecision and caution is required when interpreting the data.

Table 3.10: Analysis comparison I: Intensity of glycaemic control – strict glycaemic targets versus liberal glycaemic targets. Outcome 2: Use of pharmacological therapy



No data were reported for any of the other maternal secondary outcomes for this review (maternal mortality; weight gain during pregnancy; placental abruption; induction of labour; perineal trauma; postpartum haemorrhage; postpartum infection requiring use of antibiotics (variously defined); maternal hypoglycaemia; glycaemic control during/end of intervention (as defined by trialists); use of pharmacological treatment (oral hypoglycaemic); relevant biomarker changes associated with the intervention (including adiponectin, free fatty acids, triglycerides, high density lipoproteins, low density lipoproteins, insulin); breastfeeding; adherence with treatment/management; sense of wellbeing and quality of life; views of the intervention; behaviour change associated with the intervention).

Long-term maternal outcomes

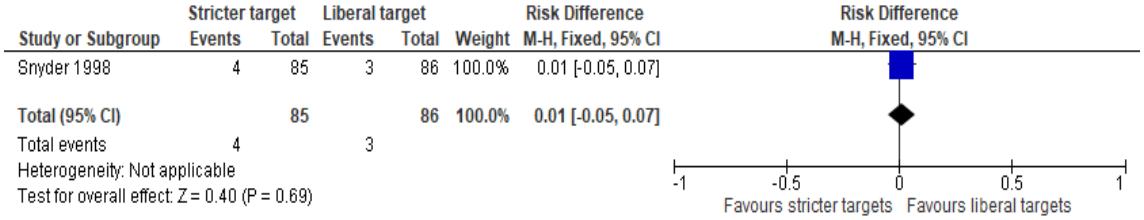
No data were reported for any of the long-term maternal outcomes for this review (postnatal depression; postnatal weight retention or return to pre-pregnancy weight; BMI; GDM in a subsequent pregnancy; type 1 diabetes mellitus; impaired glucose tolerance; cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)).

Infant outcomes

There were no clear differences for babies born to women receiving *strict* glycaemic targets for insulin treatment when compared to babies born to women receiving *liberal* glycaemic targets for insulin treatment for:

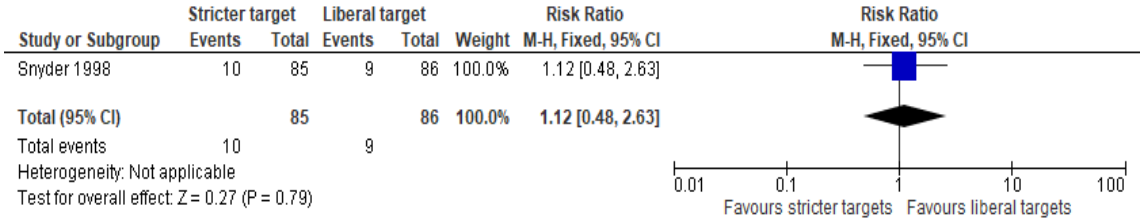
- **macrosomia** (birthweight > 4000 g) RR 1.35, 95% CI 0.31 to 5.85; one trial, 171 babies, (Table 3.8; Table 3.11);

Table 3.11: Analysis comparison I: Intensity of glycaemic control – strict glycaemic targets versus liberal glycaemic targets. Outcome 3: Macrosomia



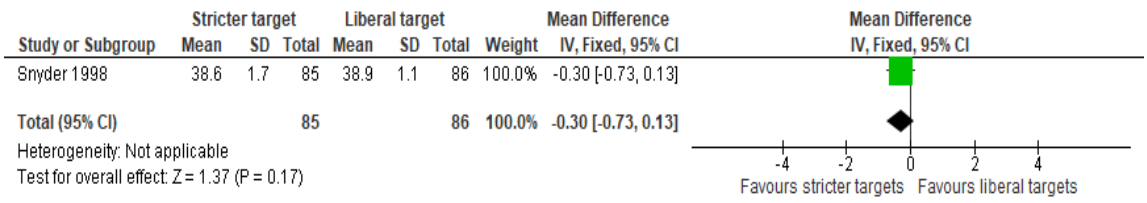
- **small-for-gestational age** RR 1.12, 95% CI 0.48 to 2.63; one trial, 171 babies, (Table 3.8; Table 3.12);

Table 3.12: Analysis comparison I: Intensity of glycaemic control – strict glycaemic targets versus liberal glycaemic targets. Outcome 4: Small-for-gestational-age



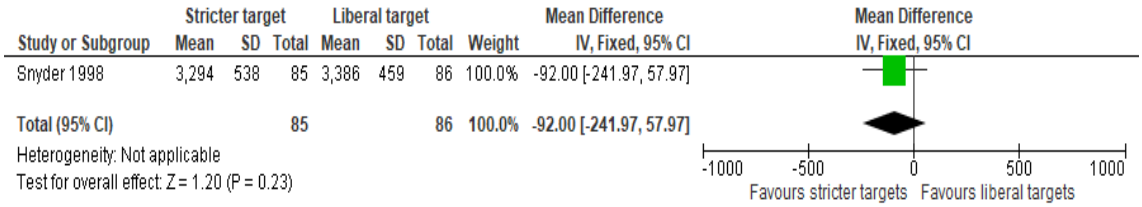
- **gestational age at birth mean difference** (MD) -0.30 weeks, 95% CI -0.73 to 0.13; one trial, 171 babies, (Table 3.8; Table 3.13);

Table 3.13: Analysis comparison I: Intensity of glycaemic control – strict glycaemic targets versus liberal glycaemic targets. Outcome 5: Gestational age at birth (weeks)



- **birthweight** MD -92.00 g, 95% CI -241.97 to 57.97; one trial, 171 babies, (Table 3.8; Table 3.14).

Table 3.14: Comparison I: Intensity of glycaemic control – strict glycaemic targets versus liberal glycaemic targets, Outcome 6: Birthweight



No data were reported for any of the other neonatal outcomes for this review (stillbirth; neonatal death; shoulder dystocia; bone fracture; nerve palsy; preterm birth (< 37 weeks' gestation; < 32 weeks' gestation); birthweight z score; head circumference and z score; length and z score; ponderal index; hypoglycaemia; respiratory distress syndrome; hyperbilirubinaemia; hypocalcaemia; adiposity; polycythaemia; Apgar score < seven at five minutes; relevant biomarker changes associated with the intervention).

Later childhood outcomes

No data were reported for any of the childhood outcomes for this review (weight and z score; height and z score; head circumference and z score; adiposity (including BMI, skinfold thickness); blood pressure; type 1 diabetes mellitus; type 2 diabetes mellitus; impaired glucose tolerance; dyslipidaemia or metabolic syndrome; educational achievement).

Adulthood outcomes

No data were reported for any of the adulthood outcomes for this review (weight; height; adiposity (including skinfold thickness, fat mass); cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome); type 1 diabetes mellitus; type 2 diabetes mellitus; impaired glucose tolerance; dyslipidaemia or metabolic syndrome; employment, education and social status/achievement).

Health services outcomes

No data were reported for any of the health service outcomes for this review (number of antenatal visits or admissions; number of hospital or health professional visits (including midwife, obstetrician, physician, dietician, diabetic nurse); admission to neonatal intensive care unit/nursery; length of antenatal stay; length of postnatal stay (maternal); length of postnatal stay (baby); cost of maternal care; cost of offspring care; costs associated with the intervention; costs to families associated with the management provided).

3.2.5 Discussion

Summary of main results

The effect of different intensities of glycaemic control in pregnant women with GDM for improving maternal and infant outcomes was assessed in this review. Only one study (involving 180 women) was identified that met the inclusion criteria for this systematic review (Snyder 1998). In the trial, the capillary glycaemic targets compared were: pre-prandial: 5.0 mmol/L (90 mg/dL) and at one-hour postprandial: 6.7 mmol/L (120 mg/dL) for the *strict* group and for the *liberal* glycaemic group: pre-prandial 5.8 mmol/L (104 mg/dL) and at one-hour postprandial 7.8 mmol/L (140 mg/dL). The *strict* glycaemic targets were associated with an increase in the use of insulin requirements. No clear differences were seen for any of the secondary outcomes for this systematic review. Based on the current limited data it remains unclear which glycaemic targets should be recommended for women with GDM for improving their health and the health of their babies.

Overall completeness and applicability of evidence

There is currently very limited evidence on the effectiveness of different intensities of glycaemic control in women with GDM. The available data are from one small (n = 180 women) Canadian study that has only been published as a conference abstract (Snyder 1998). The study reported no data for this reviews' primary maternal or infant outcomes. No data were available for maternal and child long-term outcomes or health service outcomes. Limited secondary outcomes for this review were reported.

Although an increased use of insulin treatment was associated with women randomised to the *strict* glycaemic control group, there are no data reported in adverse effects such as maternal hypoglycaemia.

The study recruited "women between 20-37 gestation referred for GDM who were then randomised to receive insulin at either the recommended *liberal* or *strict* criteria". It did not include other treatments for example, oral hypoglycaemic agents or diet and lifestyle interventions.

Due to one included study with small numbers of participants, receiving insulin as the only treatment option when treatment was needed and overall unclear risk of bias, the generalisability of the current evidence is very limited.

Four ongoing trials were identified and data from these studies, when published, will be included in future updates of this systematic review (Table 3.2).

Quality of the evidence

For the one included study, random sequence generation and allocation concealment were judged to be unclear due to lack of detail. Performance bias was judged to be of high risk as the study was unlikely to have been blinded. There was insufficient detail to make a judgement about detection bias. Attrition bias was judged to be unclear as of the 180 women recruited, outcome data were available for 171 women and babies. The reasons for the missing participants were not explained. Selective reporting was judged to be of high risk as the conference abstract is likely to have reported on a selection of outcomes from the study rather than the pre-specified study outcomes. The study was only reported as a conference abstract and no full publication was found.

We graded the quality of the evidence for caesarean section as *very low* due to poor reporting of risk of bias, imprecision and publication bias. Data for the other selected outcomes for GRADE were not reported in the included study (Table 3.6; Table 3.7).

Potential biases in the review process

Systematic searches of all potential eligible trials were carried out by the Trials Search Co-ordinator for the Cochrane Pregnancy and Childbirth Group and the authors of this review. We also searched the Cochrane Pregnancy and Childbirth Group's Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) and the reference lists of the identified trials. One author was contacted for the included study via email for additional data, but no response was received. No evidence of potential bias was identified through these systematic searches for published and unpublished studies. If we identify any studies in future searches, we will assess them for potential inclusion in this review. As the quality of the included trial is unclear and outcome data are missing, a potential for bias is present. Therefore, the study results should be interpreted with caution.

Agreements and disagreements with other studies or reviews

In this review we did not find sufficient evidence to fully evaluate which intensity of glycaemic control for women with GDM was most effective for improving the health outcomes for women and their babies. Results from only one published study (Snyder 1998) are available, but the overall risk of bias from this small trial is unclear (Figure 3.2; Figure 3.3).

There is limited evidence to guide clinical practice for targets for glycaemic control for women with GDM to minimise adverse effects on maternal and fetal health. Glycaemic target recommendations from

international professional organisations for maternal glycaemic control vary widely and are reliant on consensus given the lack of high-quality evidence (ADA 2013; Metzger 2007; Nankervis 2013; Ministry of Health 2014; NICE 2015; SIGN 2014; Thompson 2013) (Table 3.1). The evidence on which these recommendations have been made is generally unclear.

Prutsky and colleagues published a systematic review that included 34 observational studies, involving 9433 women (Prutsky 2013), summarising the evidence for glycaemic targets in pregnant women with GDM, type 1 diabetes and type 2 diabetes. No relevant randomised controlled trials were identified. Twenty-six of the 34 observational studies included women with GDM. Overall, the quality of the evidence of the observational studies included was judged to be low, with the literature limited and heterogeneity amongst the studies high. The results of Prutsky's systematic review showed that a fasting glucose target of < 5.0mmol/L was associated with a significant reduction in macrosomia (P < 0.01), large-for-gestational-age infants (P = 0.01), neonatal hypoglycaemia (P = 0.01), and neonatal jaundice (P = 0.01). For the mother, there was a significant reduction in pre-eclampsia during the third trimester of pregnancy (P = 0.01) (Prutsky 2013). Based on the results from these observational studies, the authors concluded that it remains unclear whether glucose targets above or below a fasting glucose threshold of < 5.0 mmol/L offer a better balance of benefits and risks. There was insufficient evidence on postprandial measures to assess different cut-off points and health outcomes. The review authors highlighted that there have been no well-conducted large randomised controlled trials comparing any two glycaemic thresholds that report on benefits and harms for the mother and her baby. In the light of the current evidence assessed in our review, we have reached the same conclusion.

3.2.6 Authors' conclusions

Implications for practice

The overall risk of bias of the single included study was judged to be unclear as it has only been reported as an abstract and provided very little information about the study method used. Women using *stricter* glycaemic targets in the included study used more insulin therapy, which would be expected, but no data were provided for adverse effects such as maternal hypoglycaemia. There was no difference in the risk of being born small-for-gestational age. It is important to note that these findings are based on limited data from one small randomised trial with evidence of imprecision for the few published outcomes. There is currently insufficient evidence to support *strict* over more *liberal* glycaemic treatment targets for women with GDM. It will also be important to evaluate women’s views of adhering to different

glycaemic intensities and how this affected their daily life to understand and overcome impracticalities and inconveniences such as hospital clinic attendances and the effect of blood glucose monitoring.

Implications for research

Further larger high-quality trials are needed that compare different intensities of glycaemic control targets to guide the treatment of women with GDM. High-quality trials should evaluate different blood glycaemic targets to guide treatment, assess both short-term and long-term health outcomes for women and their babies, include women's experiences and assess health services costs. Four ongoing randomised controlled trials were identified and data from these studies, if published, (Ardilouze 2015; Crowther 2015; Hague 2014; Scifres 2015) (Table 3.2) will be included in future updates of this review. These trials are of varying sizes, with Ardilouze 2015, Hague 2014 and Scifres 2015 involving 30, 40 and 60 women with GDM, respectively and Crowther 2015 involving 1080 women. All trials are comparing glycaemic control targets for women with GDM. Crowther 2015, Hague 2014 and Scifres 2015 are using the same glycaemic targets for their intervention group (5.0 mmol/L (90 mg/dL) pre-prandial and at two hours postprandial 6.7 mmol/L (120 mg/dL)). Non-numerical terms used to describe the intervention range from 'normal', 'standard care', 'low', 'less tight', 'tight' to 'very tight' and 'intensive therapy'.

3.2.7 Plain Language Summary

What is the most effective blood sugar range to guide treatment for women who develop gestational diabetes mellitus (GMD) in their pregnancy?

What is the issue?

Up to a quarter of pregnant women develop gestational diabetes mellitus (GDM) depending on their ethnicity and the diagnostic criteria used. GDM is evident as high blood sugar levels (hyperglycaemia) during pregnancy and is associated with an increased risk of developing high blood pressure (hypertension) and protein in the urine during pregnancy (pre-eclampsia). These women are more likely to have a caesarean birth, develop type 2 diabetes, postnatal depression, and cardiovascular disease later on in life. The high blood sugar levels that are associated with GDM often return to normal as soon as the baby is born, but women with GDM are at risk of again developing GDM in future pregnancies. Babies whose mothers have been diagnosed with GDM are at an increased risk of having a birthweight greater than 4000 g, increased risk of birth trauma because of their size and developing breathing difficulties after birth. The babies are also at risk of future obesity and type 2 diabetes.

Why is this important?

Women with GDM are treated with the aims of controlling high maternal blood sugar levels and reducing the risks of GDM for the mother and the baby. Blood sugar control is monitored by measuring blood sugar concentrations to ensure they are maintained within a pre-defined level or range. The blood sugar results are usually obtained by the mother using a finger prick to collect a drop of her blood on a test strip, which is inserted into a small machine (a glucometer) that reads the sugar level of the blood on the test strip. The glucometer reading alerts the pregnant woman to her current blood sugar level and is used to guide her treatment. For example, how many units of insulin she requires before eating. However, it is currently unclear how to advise pregnant women with newly diagnosed GDM what is the most effective blood sugar range to aim for and guide treatment.

What evidence did we find?

We searched for evidence on 31 January 2016 and found one small randomised controlled trial (abstract only) that was of poor quality and involved 180 women from Canada. The trial compared two blood sugar ranges, one strict the other more liberal, and reported a very few health outcomes for the pregnant woman and her baby.

The trial did not provide any data for this review's main outcomes. For the woman, these related to the development of high blood pressure and protein in the urine during pregnancy, developing type 2 diabetes. For the baby, these outcomes related to death of the baby, increased birthweight, increased risk of birth trauma because of their size, and disability.

More women were on insulin in the strictly controlled group (but this result is based on very low-quality evidence). No clear differences were reported for caesarean section rates. No other secondary outcome data for women with GDM relevant to this review were reported. No differences were reported for the number of babies that had a birthweight greater than 4000 g or were small-for-gestational age. No other secondary outcomes for the babies relevant to this review were reported. The study did not report on adverse events.

What does this mean?

This review found that there is not yet enough evidence from randomised controlled trials to determine the best blood sugar range for improving health for pregnant women with GDM and their babies. Four

studies are ongoing but not yet complete. More high-quality studies are needed that compare different targets for blood sugar levels and assess both short-term and long-term health outcomes for women and their babies to guide treatment. Studies should include women's experiences and assess health services costs.

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As part of the pre-publication editorial process, this review has been commented on by four peers (an editor and three referees who are external to the editorial team), a member of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

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Contributions of authors

Tineke Crawford (TC) and Julie Brown (JB) were both involved in conceiving the review. TC was responsible for preparing the initial draft of the protocol and designing the search strategies. JB and Caroline Crowther (CC) assisted in the preparation of the protocol. Jane Alsweiler (JA) and Ruth Martis (RM) provided additional comments and feedback.

RM and JB were responsible for the preparation of the review. JA, TC and CC provided feedback and comments throughout the preparation of the review.

Declarations of interest

Caroline Crowther, Julie Brown and Jane Alsweiler are principal investigators, and Ruth Martis is a doctoral student on the TARGET randomised controlled trial examining optimal glycaemic targets for GDM which is currently ongoing. None of the authors associated with the TARGET randomised

controlled trial will be involved in data extraction or assessment of risk of bias. Tineke Crawford will lead the data extraction for TARGET and we will seek assistance from another researcher not associated with the trial.

Differences between protocol and review

The published protocol listed seven maternal and child outcomes together to be assessed for quality using the GRADEpro approach. This has now changed for this review to seven outcomes each, maternal and child (as neonate, child, adult). The authors identified that mother and child outcomes needed to be assessed for quality separately.

We have modified some of the outcomes for this review based on consensus between the review authors and other review authors of Cochrane reviews for treatment of GDM. The outcomes are now in line with the updated outcomes across GDM reviews.

Primary outcomes

For the mother - caesarean section was amended from being a primary outcome to a secondary outcome. Pre-eclampsia was amended to hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension and eclampsia). Subsequent development of type 2 diabetes was moved from a long-term maternal outcome to a primary outcome.

For the infant - death or severe morbidity (variously defined by trials, e.g. infant death, shoulder dystocia, bone fracture or nerve palsy) was amended from a secondary outcome to a primary outcome.

Secondary outcomes

Deleted outcomes

The following maternal secondary outcomes were deleted: mode of birth (normal vaginal birth, operative vaginal birth, caesarean section); hyperglycaemia requiring changes in management during pregnancy; diabetic ketoacidosis; anxiety.

The following long-term maternal secondary outcomes were deleted: postnatal glucose tolerance; development of type 2 diabetes mellitus; hypertension; blood lipids.

The following neonatal secondary outcomes were deleted: death in infancy or childhood; congenital fetal anomaly; Z scores of birthweights, head circumference, length; neonatal infection; neonatal hyperglycaemia.

The following later childhood secondary outcomes were deleted: appropriate weight for age; anthropometry (weight, height, head circumference, adiposity, skinfold thickness, fat mass); developmental delay (variously defined by individual trials).

The following health service outcome was deleted: length of stay in neonatal intensive care unit/nursery.

Amended outcomes

The following maternal secondary outcomes were amended: hypoglycaemia requiring treatment during pregnancy amended to maternal hypoglycaemia. Glycaemic control achieved (e.g. blood glucose or HbA1c concentrations) (proportion of blood glucose concentrations within target) amended to glycaemic control during/end of intervention (as defined by trialists). Satisfaction with treatment/management amended to views of the intervention; postnatal weight retention amended to postnatal weight retention or return to pre-pregnancy weight. Postnatal depression was moved to long-term maternal outcomes.

The following neonatal secondary outcomes were amended: preterm birth amended to preterm birth (< 37 weeks' gestation; < 32 weeks' gestation); birthweight, head circumference and length amended to birthweight and z score; head circumference and z score and length and z score. Fetal adiposity amended to adiposity; neonatal hypoglycaemia amended to hypoglycaemia (variously defined).

The following adulthood secondary outcomes were amended: metabolic syndrome was amended to dyslipidaemia or metabolic syndrome; glucose tolerance/type 2 diabetes mellitus was amended to type 1 diabetes, type 2 diabetes, Impaired glucose tolerance. Blood pressure and blood lipids were amended to cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome).

The following health service secondary outcomes were amended: maternal antenatal admission amended to length of antenatal stay; additional requirements for families (such as change of diet, exercise, extra antenatal visits, glucose monitoring and strips) amended to costs to families associated with the management provided. Use of healthcare services in pregnancy (consultations, blood glucose monitoring, length and number of antenatal visits, and to whom - midwife/obstetrician/physician) amended to number of antenatal visits or admissions and number of hospital or health professional visits (including midwife, obstetrician, physician, dietician, diabetic nurse).

Additional outcomes

The following maternal secondary outcomes were added: behaviour change associated with the intervention; relevant biomarker changes associated with the intervention (including adiponectin, free fatty acids, triglycerides, high density lipoproteins, low density lipoproteins, insulin); sense of wellbeing and quality of life.

The following long-term maternal secondary outcomes were added: GDM in a subsequent pregnancy; type 1 diabetes mellitus; impaired glucose tolerance; cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome).

The following neonatal secondary outcomes were added: Apgar score < seven at five minutes; polycythaemia; relevant biomarker changes associated with the intervention (including cord c peptide, cord insulin).

The following later childhood secondary outcomes were added: weight and z score; height and z score; head circumference and z score; adiposity (including body mass index (BMI), skinfold thickness); blood pressure; type 1 diabetes mellitus; type 2 diabetes mellitus; impaired glucose tolerance; dyslipidaemia or metabolic syndrome; educational achievement.

The following adulthood secondary outcomes were added: weight, height, adiposity (including BMI, skinfold thickness); employment, education and social status/achievement.

The following health service secondary outcomes were added: costs associated with the intervention; length of postnatal stay (baby)

Subgroup analysis and investigation of heterogeneity. Within the methods for subgroup analysis, the following subgroup has been added:

4. Woman's ethnicity as identified from the trials

Chapter 4: Quantitative study identifying barriers and enablers among women with gestational diabetes mellitus

4.1 Preface

This chapter is a manuscript published by the Journal of Diabetes Research entitled **'Views and experiences of New Zealand women with gestational diabetes in achieving glycaemic control targets. The VIEWS study'.** This study reports the results of a survey administered to sixty women diagnosed with gestational diabetes mellitus (GDM) to identify existing barriers and enablers to achieving optimal capillary blood glucose control.

This study addressed the overarching research question of: What do women with GDM say are the barriers and enablers for their glycaemic targets and are there any differences of barriers and enablers identified for women with GDM between less tight and tighter glycaemic targets from a quantitative research perspective?

The chapter contains the unaltered published manuscript. The abstract and key words were removed as directed by the University of Auckland (2016) *Guide to thesis and dissertations*.

4.2 Views and experiences of New Zealand women with gestational diabetes in achieving glycaemic control targets. The Views Study.

4.2.1 Introduction

Globally there are increasing rates of diabetes, including gestational diabetes mellitus (GDM) (Wild 2004; Ministry of Health 2014). The prevalence of GDM varies among populations but probably affects 10–25% of pregnancies (Guariguata 2014; Kampmann 2015; WHO 2016).

Short- and long-term health risks for women with GDM include pre-eclampsia, induction of labour, caesarean section, and postnatal depression for the women (Metzger 2008; Nicklas 2013; NICE 2015). For the baby health risks include shoulder dystocia, nerve palsy, preterm birth, neonatal hypoglycaemia, respiratory distress syndrome and the risk of developing obesity and type 2 diabetes (T2DM) in childhood (Lucas 1988; Mitanchez 2015a; Ornoy 2015).

Treatments for women with GDM that maintain glycaemic control within specified targets have a significant impact on short- and long-term health for the woman and her baby (Crowther 2005; Landon 2009; Poolsup 2014). Treatments for GDM include dietary and exercise advice alone or combined with pharmacological therapy (Kalra 2013; Kavitha 2013; Ryu 2014; Brown 2017; Nachum 2017).

While some published studies have described women's experiences of developing GDM (Bandyopadhyay 2011a; Hirst 2012; Lapolla 2012; Trutnovsky 2012; Morrison 2014; Parsons 2014), little is known as to how women feel about achieving their glycaemic treatment targets. This nested study within the TARGET trial (Australian New Zealand Trial Registry: ACTRN12615000282583) aimed to explore women's views and experiences in achieving their recommended glycaemic treatment targets and to identify potential barriers and enablers.

4.2.2 Materials and Methods

Participant Selection

Women diagnosed with GDM were eligible to participate if they had a singleton pregnancy, could communicate in English, had been self-monitoring their capillary blood glucose concentrations for at least two weeks and provided written consent. Eligible women were sent an email invitation that included a participant information sheet and consent form. Women could choose to be interviewed face-to-face,

or to be telephoned. Women were aware that the survey was not an assessment of their knowledge about GDM and advised that all their information would be kept confidential.

Hospital sites from two different geographical locations in New Zealand participated. Twenty women, recruited from Canterbury District Health Board (DHB) in the South Island, were using less tight glycaemic treatment targets (fasting blood glucose <5.5 mmol/L; 1-hour postprandial <8.0 mmol/L; 2-hours postprandial <7.0 mmol/L). Forty women were using tighter glycaemic treatment targets (fasting blood glucose ≤5.0 mmol/L; 1-hour postprandial ≤7.4 mmol/L; 2-hours postprandial ≤6.7 mmol/L); twenty women recruited from Canterbury DHB in the South Island and twenty women recruited from Counties Manukau DHB, in the North Island.

Local hospital policies differed for testing of capillary blood glucose. Canterbury DHB moved from initially less tight targets to tighter glycaemic treatment targets during the survey time. Women were asked to test their capillary blood glucose at one-hour postprandial. Counties Manukau DHB was using tighter glycaemic treatment targets during the survey time. Women were asked to test their capillary blood glucose two-hours postprandial.

The Survey

The survey comprised 45 questions. Twenty questions identified participant demographics and twenty-five their views and knowledge of their glycaemic treatment targets. Questions included identifying what had been helpful in learning how to self-monitor capillary blood glucose concentrations, support received from family, friends and health professionals, access to written information, costs associated with their GDM management and treatment, and experience of hunger. The survey was piloted with three women following which three questions were modified. There was an opportunity for women to provide additional information. All women answered all the survey questions.

Analysis

Data analysis was conducted using Pivot Tables in Microsoft Office Excel 2016 calculating frequency and corresponding percentage to describe the responses to the survey questions and included mean and standard deviation for normally distributed data. All analyses were undertaken in Microsoft Office Excel 2016, reporting descriptive statistics for baseline demographics and using simple numeric calculations for survey responses.

Ethical Approval

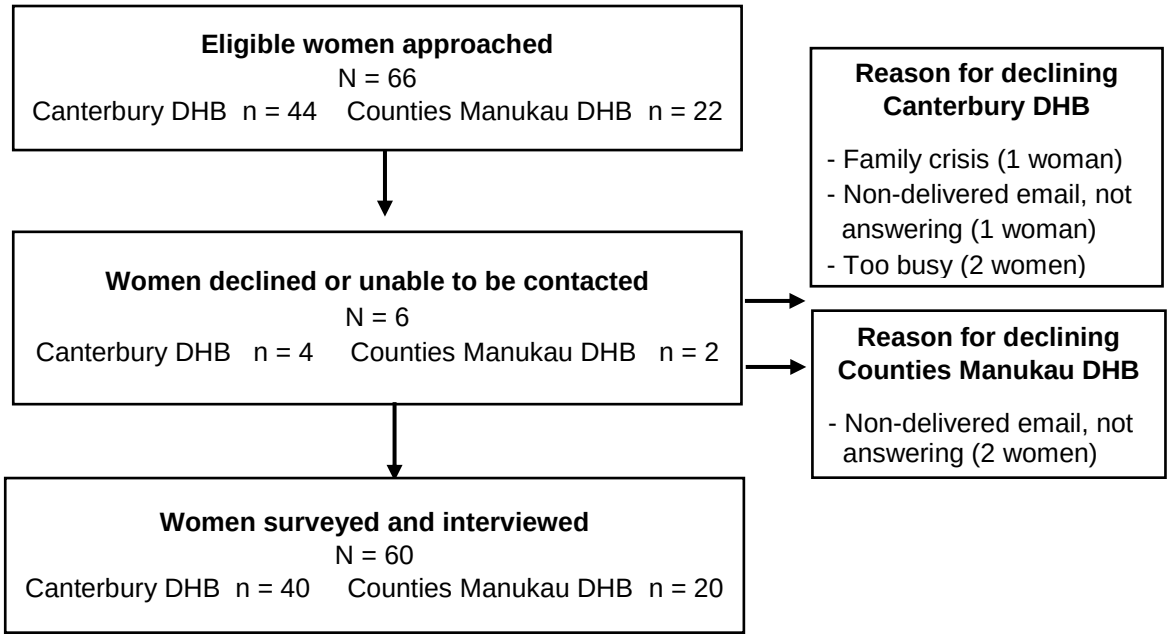
The VIEWS Survey was nested within the TARGET Trial approved by the New Zealand Health and Disability Ethics committee (HDEC) Ref. 14/NTA/163 and research registration number 1965.

4.2.3 Results

Participants

Sixty-six eligible women were approached and sixty women consented to participate in the survey. Six women did not participate because they were too busy, having a family crisis or not responding to the invitations (Figure 4.1).

Figure 4.1: Flowchart of recruitment



Face-to-face surveys were conducted with 34 (57%) women and 26 (43%) of women chose to be surveyed by telephone. The average age of participating women was 33 years (standard deviation (SD) ± 4.5). Just under half of the women (27, 45%) were primigravid, had a family history of diabetes (27, 45%) and two-thirds were classified as obese or overweight in early pregnancy (39, 65%) (Table 4.1). Most women were European (24, 40%) followed by Asian ethnicity (22, 37%). Women taking part were evenly distributed across the deprivation index: 18 (30%) women least deprived (level 1-3), 19 (32%) women (level 4-6) and 22 (37%) women most deprived (level 7-10) (Table 4.1). The demographics of the participating women are reflective of a cross section of the demographics of New Zealand's pregnant population (Census Count 2013; Counties Manakau Count n.d.; Canterbury Count n.d.).

Women were diagnosed with GDM at a mean of 27.8 ±2.0 weeks' gestation. At the time of the survey participants had been checking their daily capillary blood glucose for an average of 6.8 ±2.3 weeks (Table 4.1), with just over half checking their blood glucose four times a day (32, 53%) and the other participants six times a day (28, 47%). Ten women (17%) reported having a diagnosis of GDM from a previous pregnancy. Almost a third of women (18, 30%) were treated with diet alone; the remainder received a combination of dietary advice and medications. Thirteen (22%) women were treated with subcutaneous insulin for their GDM, 17 (28%) women metformin and 12, 20% women were treated with insulin and metformin (Table 4.1).

Table 4.1: Demographic characteristics of women who participated in the survey

Characteristics	**Women with less tight* glycaemic targets** **n=20 (% or ± of 20)**	**Women with tighter** glycaemic targets** **n=40 (% or ± of 40)**	**Women total** **N=60** **(% or ± of 60)**
Age (years)†	34 (±4.3)	32 (±4.5)	33 (±4.5)
Primigravida (G_1P_0)	9 (45)	18 (45)	27 (45)
BMI category‡			
- Normal	8 (40)	13 (32.5)	21 (35)
- Overweight	5 (25)	6 (15)	11 (18.3)
- Obese (Class I)	2 (10)	9 (22.5)	11 (18.3)
- Obese (Class II)	2 (10)	6 (15)	8 (13.3)
- Obese (Class II)	3 (15)	6 (15)	9 (15)
- Total obese	7 (35)	21 (52.5)	28 (46.6)
Ethnicity§			
- European	12 (60)	12 (30)	24 (40)
- Māori	-	6 (15)	6 (10)
- Asian	7 (35)	15 (37.5)	22 (36.7)
- Pacific Peoples	-	7 (17.5)	7 (11.6)
- MELAA	1 (5)	-	1(1.7)
Highest educational qualifications after leaving school◊			
1. No qualification	1 (5)	2 (5)	3(5)
2. Level 1 certificate	-	2 (5)	2 (3.3)
3. Level 2 certificate	2 (10)	2 (5)	4 (6.7)

Characteristics	Women with less tight* glycaemic targets n=20 (% or ± of 20)	Women with tighter** glycaemic targets n=40 (% or ± of 40)	Women total N=60 (% or ± of 60)
4. Level 3 certificate	2 (10)	4 (10)	6 (10)
5. Level 4 certificate	-	4 (10)	4 (6.7)
6. Level 5 and level 6 diploma	4 (20)	9 (22.5)	13 (21.7)
7. Bachelor degree and level 7 qualification	8 (40)	17 (42.5)	25 (41.6)
8. Post-graduate and honours degree	1 (5)	-	1 (1.7)
9. Master degree	2 (10)	-	2 (3.3)
NZ Deprivation index[◈]			
- 1 (least deprived)	3 (15)	5 (12.5)	8 (13.5)
- 2	2 (10)	3 (7.5)	5 (8.4)
- 3	2 (10)	3 (7.5)	5 (8.4)
- 4	4 (20)	6 (15)	10 (16.7)
- 5	2 (10)	5 (12.5)	7 (11.8)
- 6	1 (5)	1 (1.7)	2 (3.4)
- 7	2 (10)	3 (7.5)	5 (8.5)
- 8	3 (15)	3 (7.5)	6 (10)
- 9	1 (5)	4 (10)	5 (8.7)
- 10 (most deprived)	-	6 (15)	6 (10)
Lead Maternity Carer (LMC)[◈]			
- Midwife	19 (95)	36 (90)	55 (91.7)
- Obstetrician	1 (5)	-	1 (1.7)
- Hospital Team	-	4 (10)	4 (6.7)
Gestational age at GDM diagnosis[†] (weeks)	27.7 (±1.9)	27.9 (±2.0)	27.8 (±2.0)
Time of self-testing capillary blood glucose for (weeks)[†]	7.6 (±2.5)	6.4 (±2.1)	6.8 (±2.3)
Previous GDM	4 (20)	6 (15)	10 (16.7)
Previous hypertension	2 (10)	-	2 (3.3)
Current hypertension	-	3 (7.5)	3 (5)
Family history of hypertension	8 (45)	16 (40)	24 (40)

Characteristics	Women with less tight* glycaemic targets n=20 (% or ± of 20)	Women with tighter** glycaemic targets n=40 (% or ± of 40)	Women total N=60 (% or ± of 60)
Family history of diabetes	7 (35)	20 (50)	27 (45)
Current smoker	-	3 (7.5)	3 (15)
Current treatment			
- Diet only	7 (35)	11 (27.5)	18 (30)
- Insulin and diet	2 (10)	11 (27.5)	13 (21.7)
- Metformin and diet	5 (25)	12 (30)	17 (28.3)
- Insulin, Metformin, and diet	6 (30)	6 (15)	12 (20)

Figures are number and percentage.
*Less tight glycaemic treatment targets for women with GDM: fasting blood glucose <5.5 mmol/L; 1 hour postprandial <8.0 mmol/L; 2 hours postprandial <7.0 mmol/L.
**Tighter glycaemic treatment targets for women with GDM: fasting blood glucose ≤5.0 mmol/L; 1 hour postprandial ≤7.4 mmol/L; 2 hours postprandial ≤6.7 mmol/L.
†Mean and standard deviation.
‡BMI categories: Underweight < 18.50; Normal range: ≥ 18.55 - 24.99; Overweight: ≥ 25.00–29.99; Obese (Class I) ≥ 30.00–34.99; Obese (Class II): Severe obese ≥ 35.00–39.99; Obese (Class II): Morbid obese: ≥ 40.00 according WHO 2000 and Ministry of Health 2015 categories.
§as categorised by New Zealand government statistics groups for major ethnic groups. MELAA is an acronym for Middle Eastern/Latin American/African. http://www.stats.govt.nz/Census/2013-census/profile-and-summary-reports/infographic-culture-identity.aspx
◊as categorised by New Zealand government statistics groups. http://www.stats.govt.nz/Census/2013-census/profile-and-summary-reports/qstats-education-training/highest-qualification.aspx
◈as categorised by New Zealand 2013 Deprivation Index, University of Otago, Department of Public Health. *Deprivation score was unknown for one woman, as her address had no meshblock listed* http://www.otago.ac.nz/wellington/departments/publichealth/research/hirp/otago020194.html
◈A lead maternity carer (LMC) in New Zealand provides lead maternity care (is in charge). This can be either a Midwife, Obstetrician, or GP. https://www.midwife.org.nz/in-new-zealand/contexts-for-practice

Views and experiences about achieving recommended glycaemic treatment targets

The majority of women correctly identified their glycaemic treatment targets (59, 98%) and viewed it as very important or important to try to adhere to these targets (Table 4.2).

Documenting the blood glucose results were viewed as less important (56, 93%) compared to viewing adherence to the targets because women knew the results could be downloaded from the glucometer. These findings were similar across participants regardless of their glycaemic treatment targets (Table 4.2).

Almost two thirds of women (37, 62%) described achieving their morning fasting glycaemic target as most difficult. These findings were similar across participants, regardless of their recommended glycaemic targets (12, 60% for less tight targets and 25, 62.5% for tighter targets) (Table 4.2). The next most frequent difficulty reported for women to achieve their recommended glycaemic targets was after

their evening meal (11, 18%). Again, these findings were similar across participants regardless of their glycaemic targets (Table 4.2). Almost two thirds of women (37, 62%) experienced being always or frequently hungry (Table 4.4).

Table 4.2: Participants views and experiences of capillary blood glucose monitoring

	Women with less tight glycaemic targets n=20 (% of 20)	Women with tighter glycaemic targets n=40 (% of 40)	Women total N=60 (%)
Knew their glycaemic targets	19 (98.3)	40 (100)	59 (98.3)
Viewed achieving their glycaemic targets as very important or important	20 (100)	39 (97.5)	59 (98.3)
Viewed documenting capillary blood glucose results as very important or important	18 (90)	37 (92.5)	56 (93.3)
Experienced difficulty achieving their fasting glycaemic target before breakfast	12 (60)	25 (62.5)	37 (61.6)
Experienced difficulty with achieving their postprandial glycaemic target after dinner	3 (15)	8 (20)	11 (18.3)

Enablers to achieving optimal blood glucose control

Participants were asked to identify what helped them when learning to test their capillary blood glucose concentrations. All 60 (100%) women indicated that the health professional demonstrating collection capillary blood glucose on themselves and then watching the participant perform it was helpful (Table 4.3). Fifty-six (93%) women opted to comment further about other factors that they felt were helpful for learning self-monitoring of blood glucose. These related mainly to group or individual teaching (Table 4.3). Forty-four (79%) of the women who commented further stated that they found group sessions helpful with some women explaining that they enjoyed talking to other women and recognising that they are not alone living with GDM (Table 4.3).

A smaller proportion of women (12, 21%) received additional one to one teaching sessions and enjoyed them as it enabled them to ask ‘stupid’ questions, could slow the teacher down when English was the second language, or they felt less as though ‘mass produced’, and treated more as an individual (Table 4.3). Over a third of women (22, 37%) identified Google as a helpful tool. It is unclear which websites they visited and in which language (Table 4.3).

Support from family, friends and work colleagues was seen as enabling for achieving glycaemic control. Over half of the women 33 (55%) indicated that they found it helpful to be asked about their capillary blood glucose concentrations and being reminded to do them by partners, their children, extended family members and work colleagues (Table 4.3). Having their meals cooked by either their partners or extended family members, who incorporated the GDM diet recommendations, was found to be helpful by nearly half of the women (28, 47%) (Table 4.3). Comments indicated that this enabled women to eat more vegetables and stopped them from buying confectionary or sugar-sweetened beverages (fizzy drinks). Further comments around supportive provision of food by others included colleagues organising healthy morning teas at work and friends providing healthy food choices for baby showers. While nearly two thirds of women (37, 62%) indicated that the cost associated with the GDM diagnosis, such as food, petrol or child care, stayed the same, some women (8, 13%) reported reduced food costs since being diagnosed with GDM as an enabler due to buying fewer take-away meals (fast foods) (Table 4.3).

All women attended Diabetes in Pregnancy Services where they saw a range of health professionals. Most women (47, 78%) attended the clinic fortnightly. Support from health professionals was valued. Over two thirds of the women (41, 68%) appreciated that health professionals took time to listen and explain (Table 4.3). One (1.7%) woman could email the endocrinologist for advice and appreciated their prompt response.

Table 4.3: Enablers identified by women with GDM[1]

Enablers	Women with less tight glycaemic targets n=20 (% of 20)	Women with tighter glycaemic targets n=40 (% of 40)	Women total N=60 (%)
Health professional demonstrating on themselves CBGT[2]	20 (100)	40 (100)	60 (100)
Watching participants perform CBGT[2]	20 (100)	40 (100)	60 (100)
Group teaching	11 (55)	33 (82.5)	44[3] (78.5)
One to one teaching	6 (30)	6 (15)	12[3] (21.4)
Health professionals listening and explaining	6 (30)	35 (87.5)	41 (68.3)
Being ask about their CBGC[4] and reminded to do them	7 (35)	26 (65)	33 (55)
Others cooking incorporating GDM diet	11 (55)	17 (42.5)	28 (46.6)
Using Google	9 (45)	13 (32.5)	22 (36.6)
Going for walks/exercising together	6 (30)	9 (45)	15 (25)
Less Costs	3 (15)	5 (12.5)	8 (13.3)

[1]Multiple answers were possible for this part of the survey
[2]Capillary Blood Glucose Testing
[3]Resutls from 56 women
[4]Capillary Blood Glucose Concentrations

Barriers to achieving optimal blood glucose control

All women received written information about GDM, that explained the importance of healthy eating and its effect on blood glucose and how to self-monitor capillary blood glucose concentrations. Barriers to this written information included feeling overwhelmed with the amount of written material, and not being able to read it in their first language. Women requested to receive visual information (16, 27%) rather than words for food choices, food label reading, how to perform the finger pricks for capillary blood glucose collection and how to give subcutaneous insulin injections (Table 4.4). Over half of the women (33, 55%) found it difficult that the written information was in English and wanted the health information in their first language for themselves and for their families to better understand what GDM is and what optimal capillary blood glucose control meant (Table 4.4). Hindi was the language most frequently requested (9, 27% women), followed by Samoan (6, 18% women) then Chinese and Māori each by 5 (15%) women. This reflects the ethnic diversity of this cohort of women (Table 4.1).

Over a third of women (23, 38%) reported being offered unhealthy food by family, friends, and work colleagues and their lack of understanding as a barrier to achieving optimal glycaemic control (Table 4.4).

When engaging with the Diabetes in Pregnancy Services women, just over a fifth of women (13, 22%) reported a judgemental attitude by health professionals, being impatient with them and not believing that they had tried their hardest to stay within their recommended glycaemic treatment targets as a barrier (Table 4.4). Inconsistent information by health professionals (10, 17%), never seeing the same health professional twice (8, 13%) and long waiting hours at the clinic (7, 12%), were also experienced as difficult (Table 4.4). An increased cost for buying more vegetables, fresh fruits, and wholemeal bread was reported as a barrier by a quarter of women (15, 25%) (Table 4.4).

Table 4.4: Barriers identified by women with GDM

Barriers	Women with less tight glycaemic treatment targets n=20 (% of 20)	Women with tighter glycaemic treatment targets n=40 (% of 40)	Women total N=60 (%)
Health information available only in English	8 (40)	25 (62.5)	33 (55)
Health information in words not visual	5 (25)	11 (27.5)	16 (26.6)
Being offered unhealthy food by family, friends, work colleagues	5 (25)	14 (35)	23 (38.3)

Barriers	Women with less tight glycaemic treatment targets n=20 (% of 20)	Women with tighter glycaemic treatment targets n=40 (% of 40)	Women total N=60 (%)
Impatient, not being believed and being judged by health professionals	7 (35)	6 (15)	13 (21.6)
Inconsistent information by health professionals	4 (20)	6 (15)	10 (16.6)
Never seeing the same health professional twice	3 (15)	5 (12.5)	8 (13.3)
Long waiting hours at clinic	4 (20)	3 (7.5)	7 (11.6)
Being hungry	14 (70)	23 (57.5)	37 (61.6)
Increased costs	7 (35)	8 (20)	15 (25)

4.2.4 Discussion

In this survey women with GDM identified enablers and barriers to achieving optimal glycaemic control. While achieving optimal glycaemic control was viewed as important, most women found it difficult to achieve their morning fasting glycaemic treatment targets, experienced hunger and wanted the health information in their first language or visually displayed. For most women food costs were not reported as a concern for the family budget. Being taught blood glucose testing in a group setting was considered helpful. Health professionals and family, friends and work colleagues support was valued. Barriers reported include long clinic waiting hours, inconsistent advice, judgemental attitudes, impatience and not being believed by health professionals and unhealthy food being offered by family members, friends, and work colleagues.

Health care providers recognise that teaching moments can be maximised by incorporating specific adult-learning principles and learning styles into their teaching strategies and provide written information that supports these learning styles (Russell 2006). The survey results showed participants wished to be provided with better visual information and to have written information in their own language. Most women enjoyed group teaching sessions, although some preferred one-to-one sessions.

We found no published studies reporting on the effects of providing visual learning aids for women with gestational diabetes or the impact of having the information in their first language. One mixed method study (Frøisland 2012) among young people with type 1 diabetes (T1DM) in Norway found that a pictorial diary as a mobile phone app covering the topics diet, insulin dosage, physical activity, and pre- and post-prandial glucose measurements all led to a change in the participants' applied knowledge about the management of their diabetes. This is an area requiring further research. For information to make

sense and motivate behaviour change it needs to be provided in a language best understood by the women with GDM (Bandyopadhyay 2011a; Hirst 2012; Lapolla 2012; Devsam 2013). Women identified Google as a helpful tool. Health professionals need to be aware that women will access information beyond the clinic environment and the quality of this information may vary. Diabetes in Pregnancy Services should consider how they provide health information and the content of their teaching sessions. Health literacy providing clear and relevant health messages has been identified as an effective way to help people manage their own health care (Devsam 2013; Work Base Education Trust 2014; Ministry of Health 2015a; Bhavadharini 2017). It would be challenging for Diabetes in Pregnancy services to provide the information for women with GDM in all the languages identified through this survey. The solution may be to provide increased visual information that requires little language and/or translate the written information for the languages identified. The use of trained translators has been encouraged, as family members are often unfamiliar with the health care medical terms, may find it difficult talking about sensitive matters and may have different degrees of English fluency (Gray 2013).

Achieving adequate fasting blood glucose control prior to breakfast, also known as the dawn phenomenon, (Carroll 2005) was identified as a challenge for most women in this survey, regardless whether their recommended glycaemic targets were identified as less tight or tighter. In the literature, this has been identified previously for people with T1DM and T2DM (Porcellati 2013) but we could not find any publications specifically relating to gestational diabetes. Anecdotal evidence through social media indicates that women with GDM, do find this control difficult (Gestational Diabetes UK n.d.). Various recommendations for achieving glycaemic control include subcutaneous insulin, walking after dinner, restricting carbohydrate intake at dinner time, late protein snack before bed time and staying hydrated (Sheehan 2004) but require further research for women with GDM. Two thirds of women commented on being hungry. It is unclear from the survey if this relates to women trying to lower their morning fasting blood glucose with eating less at dinner-time or eating very low carbohydrate meals. This would benefit from further exploration.

Some women identified barriers regarding health professional's attitude to not achieving adequate glycaemic control. These included judgmental attitude, not being believed when women stated that they were trying their hardest to follow all diet and pharmaceutical recommendations and seeing a different health professional at each visit receiving inconsistent information. Findings from other qualitative studies reiterate these findings (Fahy 2012; Devsam 2013; Janes 2013) and highlights the importance

for health professional to have a woman centred approach, not only focusing on blood glucose concentrations, but investing time to listen, believing what the women says is true, provide consistent information and continuity of care (Janes 2013).

Support from family, friends, and work colleagues was appreciated by the women surveyed. These results are consistent with other studies (Mayberry 2012; Miller 2013). Barrier identification included unhealthy food being offered to them by family members, friends, and work colleagues, indicating a lack of understanding. Pregnancy in Diabetes services may consider providing opportunity for family and friends to attend information sessions about GDM and its implication or include discussions about effective strategies for difficult situations at clinic appointments.

This study had some limitations. The participants were from two selected areas in New Zealand and while they were a cross-sectional representation of the demographics of the New Zealand population, this did not include women living in rural or remote areas. The findings may not be able to be generalised as different District Health Board provide care for women with GDM through different models of care.

4.2.5 Conclusions

This survey identified barriers and enablers for women with GDM in achieving optimal glycaemic control from two different geographical locations in New Zealand. The results provide insights to women's views and experiences with GDM in achieving glycaemic control targets. Two thirds of women found it difficult to achieve adequate fasting capillary blood glucose control, regardless of their recommended glycaemic targets, and identified the need for better strategies and adequate health professional and family support to manage this difficulty. Barriers for health information and literacy identified that health professionals need to consider using a women-centred and adult learning style approach, provide visual aids, provide written information in relevant languages, and include extended family members when imparting knowledge or teaching GDM related skills. Long clinic waiting hours, inconsistent advice, judgmental attitudes and not being believed by health professionals requires further consideration when providing a health care service for women with GDM. Findings from this survey will be useful for developing strategies for Diabetes in Pregnancy Services to support women with GDM in achieving their glycaemic control.

Conflict of interest

None of the authors have any financial conflict of interests associated with this publication. Caroline A. Crowther and Julie Brown are the lead investigators for the TARGET trial in which this study is nested.

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Authors' Contributions

Ruth Martis contributed to the conception and the design of the survey, recruited the women, conducted the survey, entered the data, performed data analysis and drafted the article and the revision of the article from co-authors' feedback. Julie Brown and Caroline A. Crowther contributed to the conception and design of the survey, provided advice on data analysis, data interpretation and commented on all drafts of the manuscript and approved the final version.

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Chapter 5: Qualitative study identifying enablers and barriers among women with gestational diabetes mellitus

5.1 Preface

This chapter is a manuscript submitted for publication to the BMC Pregnancy and Childbirth Journal entitled **'Enablers and barriers for women with gestational diabetes mellitus to achieve optimal glycaemic control – a qualitative study using the Theoretical Domains Framework'.**

This study addressed the overarching Research Question 'What are women's experiences, enablers and barriers with their glycaemic targets' from a qualitative research perspective.

Sixty women diagnosed with gestational diabetes mellitus (GDM) who had at least two weeks experience with capillary blood glucose testing completed a semi-structured interview. The results identified existing behavioural factors for women with GDM in achieving optimal glycaemic control.

This chapter contains the unaltered manuscript as it is submitted. The abstract and key words were removed as directed by the University of Auckland (2016) *Guide to thesis and dissertations*.

5.2 Enablers and barriers for women with gestational diabetes mellitus to achieve optimal glycaemic control – a qualitative study using the Theoretical Domains Framework

5.2.1 Background

In New Zealand one in eleven pregnant women is diagnosed with gestational diabetes mellitus (GDM) (ADHB 2016). Maternal hyperglycaemia associated with GDM is a potentially serious complication that can result in short- and long-term health risks for the woman and her baby (Bellamy 2009; Garrison 2015; McCance 2011; Wu 2012). Optimal blood glucose regulation within recommended glycaemic targets using lifestyle changes and/or pharmacological treatments aims to reduce or prevent the adverse outcomes associated with GDM (Crowther 2005; Landon 2009; Tieu 2010). A woman's perceptions of GDM may influence whether she embraces any lifestyle changes, complies with the recommended treatment, and achieves optimal blood glucose control (Lawrence 2011).

The New Zealand Health and Disability Commissioner has identified that consumer (a health system user) involvement is a priority in health decision making (Coney 2004). Legislation such as the Health and Disability Commissioner Act 1994 (Health and Disability Commissioner 1994), and the Health and Disability Services Consumers' Rights 1996 Code (Health and Disability Services 1996) support this. International organisations including Cochrane and the World Health Organisation (WHO) concur (Boote 2013; Morley 2016). They recommend that for any research involving consumers, their experiences should be investigated to support the research results.

In 2015 the National Institute for Health and Care Excellence (NICE) published an up-dated guideline for 'Diabetes in pregnancy: management from preconception to the postnatal period' and recommended that further robust qualitative studies were needed to explore enablers and barriers for women with GDM to maintain optimal glycaemic blood control (NICE 2015). Increased understanding of the enablers and barriers for women with GDM may help facilitate behaviour change and assist health care professionals to support women with GDM more effectively to overcome the barriers identified and support the enablers.

The use of the Theoretical Domains Framework (TDF), which informed data analysis, is an effective tool to identify enablers and barriers and to understand, inform and facilitate effective behavioural change and health service provision (Michie 2005; Michie 2008; Michie 2011). TDF was developed using an

expert consensus process and validation to identify psychological and organisational theory relevant to behaviour change (Michie 2005, Michie 2008; Michie 2011; Atkins 2017). The most recent validated version of the TDF includes 14 domains and their component constructs (Cane 2012) (Table 5.1). The TDF has been used in health care to identify factors influencing health practitioner's clinical behaviour and behaviour change (Cane 2012; Davies 2010; French 2012) but is increasingly being used to identify enablers and barriers for the consumer (user of health care) to understand their experiences and views to adherence of treatment and lifestyle changes (Burgess 2014; McGoldrick 2016; Nicholson 2014; Penn 2014).

Table 5.1: Refined Theoretical Domains Framework

Theoretical Domains	Generic Definitions	Constructs
Knowledge	An awareness of the existence of something	- Knowledge (including knowledge of condition/scientific rationale) - Procedural knowledge - Knowledge of task environment
Skills	An ability or proficiency acquired through practice	- Skills - Skills development - Competence - Ability - Interpersonal skills - Practice - Skill assessment
Social/Professional Role & Identity	A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting	- Professional identity - Professional role - Social identity - Identity - Professional boundaries - Professional confidence - Group identity - Leadership - Organisational commitment
Beliefs about capabilities	Acceptance of the truth, reality or validity about an ability, talent, or facility that a person can put to constructive use	- Self-confidence - Perceived competence - Self-efficacy - Perceived behavioural control - Beliefs - Self-esteem - Empowerment - Professional confidence
Optimism	The confidence that things will happen for the best or that desired goals will be attained	- Optimism - Pessimism - Unrealistic optimism - Identity
Beliefs about consequences	Acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation	- Beliefs - Outcome expectancies - Characteristics of outcome expectancies - Anticipated regret - Consequents
Reinforcement	Increasing the probability of a response by arranging a dependent relationship,	- Rewards (proximal/distal, valued/not valued, probable/improbable) - Incentives

Theoretical Domains	Generic Definitions	Constructs
	or contingency, between the response and a given stimulus	- Punishment - Consequents - Reinforcement - Contingencies - Sanctions
Intentions	A conscious decision to perform a behavior or a resolve to act in a certain way	- Stability of intentions - Stages of change model - Transtheoretical model and stages of change
Goals	Mental representations of outcomes or end states that an individual wants to achieve	- Goals (distal/proximal) - Goal priority - Goal/target setting - Goals (autonomous/controlled) - Action planning - Implementation intention
Memory, attention, and decision processes	The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives	- Memory - Attention - Attention control - Decision making - Cognitive overload/tiredness
Environmental context and resources	Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behaviour	- Environmental stressors - Resources/material resources - Organisational culture/climate - Salient events/critical incidents - Person × environment interaction - Barriers and facilitators
Social influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings or behaviours	- Social pressure - Social norms - Group conformity - Social comparisons - Group norms - Social support - Power - Intergroup conflict - Alienation - Group identity - Modelling
Emotion	A complex reaction pattern, involving experiential, behavioural and physiological elements, by which the individual attempts to deal with a personally significant matter or event	- Fear - Anxiety - Affect - Stress - Depression - Positive/negative affect - Burn-out
Behavioural regulation	Anything aimed at managing or changing objectively observed or measured actions	- Self-monitoring - Breaking habit - Action planning

Source: Adapted from Cane 2012 and Atkins 2017

The aims of this study were to explore the views and experiences of women with GDM with a focus on enablers and barriers to achieving optimal CBG control. Initially women were asked about how they felt and reacted when they were first diagnosed with GDM and if these impressions changed over time. To achieve the aims of the study, three broad questions were explored with participating women:

1. What is it like for a woman to monitor their CBG concentrations?

2. What affects a woman's capillary CBG concentrations and how does she maintain optimal CBG control with this knowledge?
3. What support have women found helpful/not helpful in learning about and maintaining optimal CBG control?

5.2.2 Methods

Study design and procedure

This was a qualitative descriptive study and thematic content analysis as informed by Braun and Clarke and the Theoretical Domains Framework was used to analyse the data (Braun 2006; Michie 2011; Cane 2012; Kim 2017). Semi-structured interviews enabled women with GDM to express their views and experiences in their own words (Glanz 2008; Sandelowski 2010). Women could choose to be interviewed face-to-face, or to be telephoned. Women were made aware that the interview was not an assessment of their knowledge about GDM and that they could stop the interview at any time. They were advised that all their information would be kept confidential. All women chose a pseudonym at the end of the interview for de-identifying their data and for use when disseminating the results.

This qualitative study was nested within the TARGET Trial (Optimal Glycaemic Targets for Gestational Diabetes), a stepped wedge randomised controlled trial (Australian New Zealand Trial Registry: ACTRN12615000282583), which is assessing less tight and tighter glycaemic targets for women with GDM and the effect on maternal and perinatal morbidities. The study was approved by the New Zealand Health and Disability Ethics committee (HDEC) Ref. 14/NTA/163, research registration number 1965. Locality agreements were obtained from Canterbury and Counties Manukau District Health Boards (DHB).

Study setting

Two New Zealand tertiary hospitals participated, one from the South Island (Canterbury DHB)) and one from the North Island (Counties Manukau DHB). Hospital policies differed for glycaemic targets and testing of capillary blood glucose (CBG). During the study, Canterbury DHB moved from initially less tight glycaemic targets (fasting blood glucose <5.5 mmol/L; 1-hour postprandial <8.0 mmol/L; and 2-hours postprandial <7.0 mmol/L) to tighter targets (fasting blood glucose ≤5.0 mmol/L; 1-hour postprandial ≤7.4 mmol/L; and 2-hours postprandial ≤6.7 mmol/L). Women were asked to test their CBG at one-hour postprandial. Counties Manukau DHB used tighter glycaemic targets during the study

(fasting blood glucose ≤5.0 mmol/L; 1-hour postprandial ≤7.4 mmol/L; and 2-hours postprandial ≤6.7 mmol/L) and women were asked to test their CBG two-hours postprandial.

Study participants

Women with GDM were eligible to participate if they had not yet given birth, had a singleton pregnancy, were able to communicate in English and had been self-monitoring their CBG concentrations for at least two weeks. All women with GDM recruited between August 2016 to February 2017 for the TARGET Trial at Canterbury and Counties Manukau DHB were sent an email invitation to consider participation in this nested study with a participant information sheet and consent form attached. Eligible women who wished to participate signed a consent form for this study.

Study materials

A question guide to facilitate the semi-structured interview was developed and pilot tested with three women who had GDM. This resulted in the addition of one question about hunger and adding the request for a pseudonym for identification rather than only a number to identify the data of participants. The data from these three women involved in piloting the question guide was included in the analyses. If women needed further guidance to share their thoughts, the question guide listed prompts and sub-questions for each broad question.

The semi-structured interview

One researcher (RM), with facilitating skills, conducted all the interviews over a six months' time period (August 2016 to February 2017). The woman's choice directed the place and timing of the interview. Consequently, face-to-face interviews were conducted at a variety of settings including a woman's home, work place, botanical gardens, cafés, on farms and hospital sites. No time constraints were applied for the interviews with most lasting about 40 minutes.

Data collection and analysis

All interviews were recorded using a digital recorder and were transcribed verbatim using Microsoft 2010 by independent transcribers, who had signed a confidentiality agreement. The transcripts were verified by the researcher (RM) and entered into NVivo11 for windows (QSR 2011) for data management and analysis. Thematic content analysis was conducted initially using an inductive approach (Braun 2006) where transcripts were read and re-read in full for familiarisation with the data and analysed using open coding techniques assigning a code to each meaningful segment of text. As the open codes became

saturated, a list of specific themes was generated, compared and categorised to broader overarching themes, following Braun's steps 1-5 (Braun 2006) (Table 5.2). This was followed by a deductive approach assigning the themes with meaningful text to one or more of the 14 theoretical domains reflected in the Theoretical Domain's Framework (Michie 2011; Cane 2012; Atkins 2017) (Table 5.1).

Table 5.2: Braun's (2006) Thematic Analysis Approach

Steps	Content
1. Familiarisation with the data	Reading and re-reading the data, to become immersed and intimately familiar with its content
2. Coding	Generating succinct labels (codes) that identify important features of the data that might be relevant to answering the research question. It involves coding the entire dataset, and after that, collating all the codes and all relevant data extracts, together for later stages of analysis.
3. Searching for themes	Examining the codes and collated data to identify significant broader patterns of meaning (potential themes). It then involves collating data relevant to each candidate theme, so that you can work with the data and review the viability of each candidate theme.
4. Reviewing themes	Checking the candidate themes against the dataset, to determine that they tell a convincing story of the data, and one that answers the research question. In this phase, themes are typically refined, which sometimes involves them being split, combined, or discarded.
5. Defining and naming themes	Developing a detailed analysis of each theme, working out the scope and focus of each theme, determining the 'story' of each. It also involves deciding on an informative name for each theme.
6. Writing up	Weaving together the analytic narrative and data extracts and contextualising the analysis in relation to existing literature.

Source: Adapted from Braun 2006

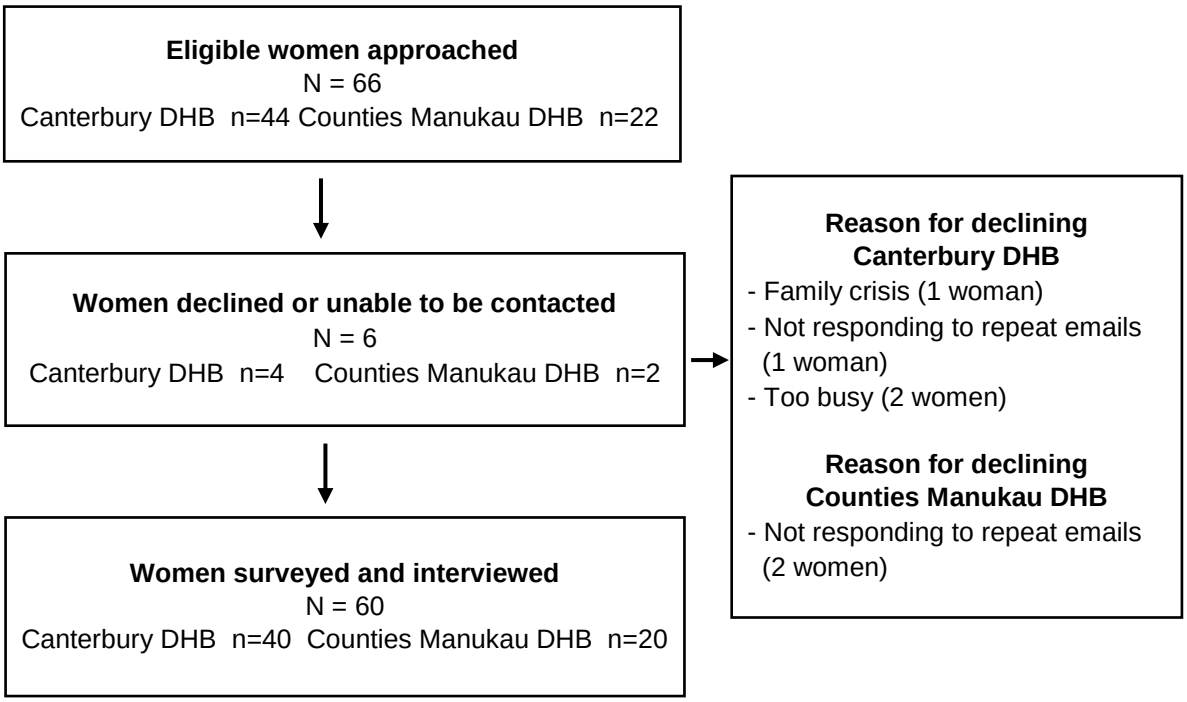
Two researchers (RM and JB) coded and classified the data and consulted with the other authors (JMC and CAC) to discuss and revise synthesising the text into the final behavioural domains with enablers and barriers identification for aspects of optimal glycaemic control. Where text fitted into multiple domains, two researchers (RM and JB) discussed and decided which text should be coded into the domain that best reflects the key theme (Atkins 2017) and whether a statement represented a barrier or enabler to achieving optimal glycaemic control. Reporting of this study was based on the COREQ (**Co**nsolidated Criteria for **Re**porting **Q**ualitative Research) checklist (Tong 2007).

5.2.3 Results

During the study period, sixty-six eligible women with GDM consecutively recruited to the TARGET Trial were approached. Six women declined to be part of this study because they were too busy, having a family crisis or did not respond to the email invitation (Figure 5.1).

Twenty women with GDM were recruited from the Counties Manukau DHB site and 40 women with GDM from Canterbury DHB site, giving a total of 60 participants.

Figure 5.1: Flowchart of recruitment



The sociodemographic characteristics of the women who participated are reflective of a cross section of the demographics of New Zealand's pregnant population (Census NZ 2013; Counties Manakau Count n.d.; Canterbury Count n.d.) (Table 5.3). Data were analysed and coded from 858 transcribed pages (249,692 words).

Women were diagnosed with GDM at a mean gestational age of 27.8 weeks (standard deviation (SD) ± 2.0. Ten women (16.7%) reported having GDM in a previous pregnancy and twenty-seven (45%) women reported a family history of diabetes (Table 5.3). When interviewed, the women had been checking their daily CBG for an average of 6.8 ± 2.3 weeks (Table 5.3). Twenty-eight women (47%) were checking their daily CBG concentration six times (before and after breakfast, lunch and dinner) and thirty-two women (53%) were checking CBG concentrations four times a day (before breakfast and after breakfast, lunch and dinner) (Table 5.3). Almost a third of women (18, 30%) were treated with diet alone. Thirteen (21.7%) women were treated with subcutaneous insulin for their GDM, 17 (28.3%) women with metformin and 12 (20%) women were treated with insulin and metformin (Table 5.3). For the interview 34 (57%) women chose to be interviewed face-to-face and 26 (43%) women by telephone (Table 5.3).

Table 5.3: Demographic characteristics of women who participated in the interviews

Characteristics	Women total n=60 (%)
Age (years)[§]	33 (±4.5)
Primigravida (G_1P_0)	27 (45)
BMI category[†]	
- Normal	21 (35)
- Overweight	11 (18.3)
- Obese (Class I)	11 (18.3)
- Obese (Class II)	8 (13.3)
- Obese (Class II)	9 (15)
- Total obese	28 (46.6)
Ethnicity[‡]	
- European	24 (40)
- Māori	6 (10)
- Asian	22 (36.7)
- Pacific Peoples	7 (11.6)
- MELAA	1(1.7)
Highest educational qualifications after leaving school[*]	
1. No qualification	3(5)
2. Level 1 certificate	2 (3.3)
3. Level 2 certificate	4 (6.7)
4. Level 3 certificate	6 (10)
5. Level 4 certificate	4 (6.7)
6. Level 5 and level 6 Diploma	13 (21.7)
7. Bachelor degree and level 7 qualification	25 (41.6)
8. Post-graduate and honours degree	1 (1.7)
9. Master degree	2 (3.3)
New Zealand Deprivation index[**]	
- 1 (least deprived)	8 (13.5)
- 2	5 (8.4)
- 3	5 (8.4)
- 4	10 (16.7)

Characteristics	Women total n=60 (%)
- 5	7 (11.8)
- 6	2 (3.4)
- 7	5 (8.5)
- 8	6 (10)
- 9	5 (8.7)
- 10 (most deprived)	6 (10)
Lead Maternity Carer (LMC)[***]	
- Midwife	55 (91.7)
- Obstetrician	1 (1.7)
- Hospital Team	4 (6.7)
Health history	
Gestational age at GDM diagnosis (weeks)[§]	27.8 (±2.0)
Previous GDM	10 (16.7)
Previous hypertension	2 (3.3)
Current hypertension	3 (5)
Family history of hypertension	24 (40)
Family history of diabetes	27 (45)
Current smoker	3 (15)
Capillary blood glucose testing (CBG)	
Weeks of self-testing capillary blood glucose at interview[§]	6.8 (±2.3)
Daily self-testing CBG: four times (Before breakfast, after breakfast, after lunch and after dinner)	32 (53)
Daily self-testing CBG: six times (Before and after breakfast, lunch and dinner)	28 (47)
Current treatment	
- Diet only	18 (30)
- Insulin and diet	13 (21.7)
- Metformin and diet	17 (28.3)
- Insulin, Metformin and diet	12 (20)
Interview type	
Face-to-face interview	34 (57)
Phone interview	26 (43)

Figures are numbers and percentages
[§]Mean and standard deviation
[†]BMI categories: Underweight < 18.50; Normal range: ≥ 18.55 - 24.99; Overweight: ≥ 25.00–29.99; Obese (Class I) ≥ 30.00–34.99; Obese (Class II): Severe obese ≥ 35.00–39.99; Obese (Class II): Morbid obese: ≥ 40.00 (according to WHO 2000 and Ministry of Health 2015 categories)

‡as categorised by New Zealand government statistics groups for major ethnic groups. MELAA is an acronym for Middle Eastern/Latin American/African. http://www.stats.govt.nz/Census/2013-census/profile-and-summary-reports/infographic-culture-identity.aspx
*as categorised by New Zealand government statistics groups. http://www.stats.govt.nz/Census/2013-census/profile-and-summary-reports/qstats-education-training/highest-qualification.aspx
**as categorised by New Zealand 2013 Deprivation Index, University of Otago, Department of Public Health. *Deprivation score was unknown for one woman, as her address had no meshblock listed* http://www.otago.ac.nz/wellington/departments/publichealth/research/hirp/otago020194.html
***A Lead Maternity Carer (LMC) in New Zealand provides lead maternity care (is in charge). This can be either a Midwife, Obstetrician, or GP. https://www.midwife.org.nz/in-new-zealand/contexts-for-practice

Women's initial response to being diagnosed with GDM

As an introduction to the interview, women were asked how they responded when diagnosed with GDM and if that response changed over time. This enabled women to share their emotions and thoughts about GDM, to recognise how far they had come on their journey with GDM and provided an effective platform for discussing enablers and barriers to achieving optimal glycaemic control (Edwards 2013). Over a third of the women described their initial response as being shocked (21, 35%).

"Shocked, I don't feel like I have diabetes, as I feel normal and okay" (Belle 19A).

Seven (11.7%) women described it as unexpected, while five (8.3%) women felt okay about the diagnosis.

"The initial gut reaction is like, oh my God, I did not expect this and what does this mean for my baby?" (Karen 09A).

"I felt okay, because I know lots of Asian people, my friends around, they are pregnant. And a lot of Asian women they very, very easily get diabetes, pregnancy diabetes. So, I am prepared. I am okay" (Casey 01A).

The remainder of women described their initial response as being disappointed (4, 6.7%), gutted (3, 5%), annoyed (3, 5%), upset (3, 5%), guilty (3, 5%), devastated (3, 5%), defeated (2, 3.3%), freaked out (2, 3.3%), angry (2, 3.3%) miffed (1, 1.7%) and heart-broken (1, 1.7%).

"I think disappointing, because my diet's pretty clean anyway. In that sense, it was disappointing" (Sian 11A).

"Can't be true, gutted, made them do another test, otherwise I would not do the treatment" (Larissa 01B).

Women's response to living with GDM at the time of the interview

Women at the time of the interview had been living with GDM for an average of 6.8 ± 2.3 weeks (Table 5.3). Most of the women commented that they had moved on from their initial response (49, 81.7%).

They accepted the diagnosis as 'okay' because it would only last a finite time, but did not like the focus on the numbers of their glycaemic targets, their CBG results, weight gain and 90th percentile of fetal growth.

"It's hard because we have to change our routine, we have to change our food patterns and all those sort of things, changing our life to be frank, but when it comes to the reality, that makes you know, a huge difference, in our life, so it's a big change, a big challenge but we have to accept it, even though the numbers run my life but we have to do the things. The other good thing after my delivery, it will go away" (Anna 07).

"It's quite overwhelming in the beginning you kind of realise now that it's not as big it kind of first seems. You just kind of adjust to it I guess and then its ok, always have to keep a look out for the numbers though" (Collette 09B).

Theoretical Domains Framework – enablers and barriers

Following Braun's (Braun 2006) (Table 5.2) thematic content analysis, the emerging themes were categorised into the TDF domains assigning the themes with meaningful text to one or more of the 14 theoretical domains (Michie 2008; Cane 2012) (Table 5.1) for enablers and barriers identification. The results are reported for each of the study questions. The 10 categorised domains, their definitions and identified enablers and barriers from women with GDM are listed in Tables 5.4 to 5.6.

What is it like for a woman to monitor her CBG concentrations?

The themes emerging from the interviews from women with GDM for the first research question 'What is it like for a woman to monitor her CBG concentrations?' were categorised within nine out of the possible fourteen TDF domains. These were: Knowledge, Skills, Beliefs about capabilities, Beliefs about consequences, Memory, attention and decision process, Environmental context and resources, Social influences, Emotion and Behavioural regulation (Table 5.4). The domains represented most strongly in the interviews in the context of this question were: Beliefs about capabilities, Social influences and Emotions.

Table 5.4: Enablers and Barriers for women with GDM to monitor their CBG concentration

Domains and Definitions	Enablers	Barriers
Knowledge Refers to a woman knowing her glycaemic targets and procedural knowledge of how to test accurately	Glycaemic targets on: - sticker on the recording booklet - post-it notes on work computer - mobile phone notebook - visual step-by-step pamphlet - list how to perform CBG testing	- different glycaemic targets to previous pregnancy - unable to read the 'how to do it list' in first language - no visual images of how to perform CBG testing
Skills Refers to a woman's ability to perform the CBG testing, working the glucometer correctly and documenting results and completing a food diary	Techniques for CBG flow: - alternating warm fingers & hands - not using soap - pricking on side of finger pads Food diary documenting	- no apps available for recording CBG results - food diary writing space too small - food diary not in first language - not knowing how to go back on glucometer
Beliefs about capabilities Refers to a woman's beliefs about her capability to perform, control and monitor her CBG concentration	- can-do attitude - perceived control of GDM - in control of CBG testing - capable of interpreting CBG results and adjusting food intake	- can't-do it attitude, too difficult - belief that it is not necessary to test regularly - perceived lack of control
Beliefs about consequences Refers to a woman's expectations about optimal CBG control	Anticipated positive consequences: - adhering to glycaemic targets will control GDM - secure healthy future for the baby - baby will be a normal size - belief future health will be better - belief family health will be better	Anticipated negative consequences: - fingerpicks damage finger pads, too difficult to play the piano or guitar - testing and controlling CBG did not work last time
Memory, attention, and decision process Refers to a woman's ability to remember when and decide where, to perform CBG testing	- mobile phone alarm reminder - setting timer on microwave - dedicated bag ready access to glucose testing equipment - able to decide where to do CBG testing	- forgetful - no reminder plan in place - unable to think outside the square - concern for doing CBG testing outside the home

Domains and Definitions	Enablers	Barriers
Environmental context and resources Refers to a woman's access to equipment and to a health professional when unsure about results	- free resources for CBG testing - phone access to diabetes midwife - booklet fits into glucometer bag - pharmacist teaching CBG testing - group teaching sessions for learning CBG testing	- costs of resources needed for CBG testing - no phone access to diabetes health professionals - booklet too big for glucometer bag - health professional not believing results
Social influences Refers to a woman's social interactions for CBG monitoring and maintaining optimal CBG control	- supportive and engaged social interactions - do it wherever, no concern - work colleagues remind them - provide healthy food at work	- social pressure and loss of choice - worried about performing CBG testing in public, being judged - being told to leave restaurant for CBG testing - work demands, meetings, unable to stop work for CBG testing
Emotion Refers to a woman's reaction/feelings to monitoring and maintaining her CBG concentrations	- privilege to have been diagnosed - enabled learning a new skill that directed positive lifestyle changes - fun doing everyone's CBG level - not as painful as anticipated	- anxiety, scared, needle phobia - stress to remember doing CBG testing, - feeling guilty when forgotten - focus on numbers not the woman - not enjoying reading
Behavioural regulation Refers to a woman's focus on self-monitoring effectively and planning how to incorporate this into her daily life	- action plan to monitor CBG - motivated by the baby to monitor CBG regularly - documenting honestly - sharing on social media glycaemic target achievements	

Knowledge

The domain 'Knowledge' in the context of monitoring optimal CBG control refers to a woman knowing her glycaemic targets and procedural knowledge of how to test accurately. Nearly all women knew their glycaemic targets and most understood the importance of adhering to them, enabling the process of performing routinely CBG testing. Enablers to assist this knowledge were identified as having information aids, such as stickers at the front of the recording booklet displaying the glycaemic targets, post-it notes for a work computer and glycaemic targets recorded on their mobile phone. Using a visual step-by-step pamphlet to ensure correctly obtaining capillary blood for glucose testing enabled procedural knowledge retention.

"I actually understood why I had to do this air tight control, so I do it. The sticker on the booklet reminds me of my numbers and the booklet in glucometer with pictures reminds me what to know" (Erin 04B).

Women reported barriers as being confused by different glycaemic targets compared to their last pregnancy with GDM and information that would have aided their procedural knowledge not being provided in enough visual detail or the information was not in their first language.

"The consultant gave me something that I haven't looked at but it was 'I quit sugar' and I wouldn't recommend that, as it sounded like sugars poison and all this kind of stuff. Pictures would be so much better" (Alice 10A).

"I think it's important to give us something to take away, and some bullet points or pictures, now that you are diagnosed, these things you need to do, why we are doing it and in the right language" (Christina 15A).

Skills

The domain 'Skills' refers to a woman's ability to perform the CBG testing, working the glucometer correctly and documenting results and completing a food diary. Women identified various effective techniques to enable good capillary blood flow and reducing discomfort. This included not using soap for washing hands (as a belief that soap contains sugar), pricking on the edge of the finger pads, placing sufficient pressure on finger pads, wiping the first blood spot off and alternating of warm fingers and hands. Keeping a food diary helped women to make a connection between what they ate and what the test results meant, encouraging the up-keep of both regular accurate testing and recording in the food diary.

"Just pressing your fingers firmly against the end of the pricky thing on the side, because no one wants to do it twice. Next time either side of the next finger and then keep going to the next finger, all makes it less painful and better blood drops" (Toni 03B).

Barriers included having a needle phobia and women feeling frustrated that a phone app for recording CBG results was not available or not being able to document into an electronically food diary. Over half of the women wanted instructions for CBG testing in their first language, the opportunity to record their food diary in their first language and more writing space in the hard copy food diary. Some women did not know how to go back on the glucometer to check their previous results. All these barriers prevented women from either mastering or performing regular glucose testing and recording their food intake.

"To be honest, the diabetes books are quite small to write in what you are eating and that can be off putting, for me I found anyway. It would so much better to have everything on my phone, like a phone app for the blood sugars and like a kind of electronic diary, everything else is on my phone, then I would do it more regularly I think" (Janet 07A).

"I think they give you a lot of information that.... I mean it's good to have. But then again, yeah, I'm probably not much of a reader. I just like to speak to thing, maybe give me a YouTube clip [link], and have picture that remind me how to, that would definitely help especially if it's your first language" (Larissa 01B)

Beliefs about capabilities

'Belief about capabilities' refers to a woman's belief about her capability to perform, control and monitor her CBG concentration. The most common reported constructs were self-confidence and having control to help women to do their CBG testing without concerns, alter their food intake accordingly and developed a 'can-do attitude'. Barriers were identified as having a 'can't-do' attitude, believing that it is not necessary to test their CBG concentrations regularly and a feeling of not being in control.

"The dietician and the doctor were very impressed with my numbers, and that made me feel amazing and proud, and chuffed with myself. I can do this" (Anneri 14B).

"It's too hard, I can't do it" (Yoko 15B).

Women who had firm beliefs about their capability reported how they were not concerned to do the CBG testing in public or at work and were highly motivated to do the testing at the appropriate times, even if it meant interrupting what they were doing.

"I am good at this", do it always on time. I do it when I am commuting on the bus or when I am attending mass. Even though I am in the middle of kneeling and everyone is quiet, I will just quickly get out my kit and quickly prick myself even though it may make some noise" (Karroll 05B).

Women with uncertain beliefs about their capabilities became increasingly scared to do their CBG testing. They had to repeat tests more often, as there was either not enough blood for the test or the glucometer would show error messages, which led them to test less often than recommended, or not at all. Women's feelings voiced of not being in control, as the CBG concentrations directed their food, exercise and/or medication intake, contributed to low self-belief in their capabilities.

"Yes, I get frustrated with it and then the glucometer does not work. Yes, I have my days where I'm tired and I'm sick of it, and belief I can't do it. I don't do my blood tests then, and I don't manage my food. It just runs my life" (Karrena 17B).

Beliefs about consequences

This domain refers to a woman's expectations about optimal CBG control. Participating women reported that anticipated positive or negative consequences strongly influenced their actions; whether they tested their CBG concentrations, adhered to the glycaemic targets, changed their food intake and physical activities, or took their medication. This domain was represented strongly throughout the interviews.

"They did tell us like that if mums are not taking care, there may be a chance for the baby to have the diabetes when the baby is a teenager or when it is little, that was a good thing, that is the one reason which I'm more careful, which I don't want to give anything to my kids which is from me you know, whatever the life brings to them that's their luck you know, but I don't want to give anything from me to my next generation, so you know, if I can be more careful about that then I have to, totally changed everything and never forget to do blood sugars" (Anna 07).

"Well, can I play the guitar with so many holes in my fingers? Who wants that? So, pricking only alternative days makes and not on my left hand is sort of ok, but if I have to play in church, I don't do it the week before" (Yasmin 01).

Memory, attention, and decision process

This domain refers to a woman's ability to remember when, and decide where, to perform CBG testing. Women identified memory aids, such as alarms on mobile phones, setting a timer and having a dedicated bag for all the CBG testing equipment to aid their memory and the decision process of performing the test, regardless of where they were. Forgetfulness was identified as a perceived barrier for doing regular CBG testing, in particular when away from their home, causing considerable frustration and anger for some women.

"Yeah husband reminds me at night most of the time (Amali 16). I get my partner to ring me and then do it. A couple of times when I've been driving I did it while I was driving" (Angela 15). "I keep my alarm on the phone, as otherwise you know, I can't remember the particular time" (Hana 11B). "Just put an alarm in my head and watch my clock every couple of hours" (Neethu 02).

"I do it anywhere… And they will ask me what are you doing? And that is the time I start talking to them about gestational diabetes and I say, 'you know I have gestational diabetes and I have to do this'. And then about at the same time I am like a tool for everybody to find out about diabetes and they learn about it" (Karroll 05B).

I tend to stress about it for the first half an hour after a meal, that I've got to remember, and then it just slips your mind some days, so frustrating (Erin 18B).

Environmental context and resources

'Environmental context and resources' refers to a woman's access to equipment and to a health professional when unsure about results. The most commonly reported barrier was the cost of resources, no phone access to a health professional when the woman was unsure about results and health professionals not believing the women's documented CBG results. Different sizes of CBG recording booklets were either experienced as enablers or barriers. Some women found it frustrating that their CBG recording booklet did not fit into the glucometer bag, which meant it had to be carried separately. This meant for some women CBG results were not recorded when outside their homes.

In New Zealand women receive a free glucometer, blood lancets, and testing strips from the diabetes in pregnancy services at their local hospital or they are given a prescription for these resources to be picked up from their local pharmacy. While some women could pay the costs of the prescription fee, some women found it too difficult over time and then did not continue CBG testing.

"It's definitely more expensive … and then prescriptions fees for the testing bits. It all adds up and you want to be sure it's worth it. Some weeks it is not" (Jean 16B).

"Yeah, like insinuating that I eat overnight, because my levels are high in the morning, like no, I am busy sleeping actually, but yeah that I struggled with, not being believed by the diabetes consultant. Why should I continue testing then?" (Alice 10A).

Social influences

In the context of this study the domain 'social influences' refers to a woman's social interactions for CBG monitoring and maintaining optimal CBG control. Engaged social interactions, such as work colleagues asking after CBG concentrations and reminding women to do their testing, as well as providing healthy food choices and stopping meetings to provide opportunity for the women to do their testing were

enablers. Barriers were being told to leave the restaurant (or other public places) when performing CBG testing and being unable to stop work for the testing. Women working as managers, bus drivers, factory workers, nurses and doctors in particular found it difficult to adhere to the post-prandial timeframes for CBG testing, as there was often little opportunity to stop their work.

"Well, at work they gave me private corner to do it [CBG testing] and they are really interested what my levels are. My colleagues remind me. So helpful" (Yoko 15B).

"I feel bad if I don't do it, but yeah it's usually as I've just been somewhere where I feel I couldn't do it, or I can't stop at work, especially now that I had the experience of being told to leave the restaurant and they think you are a druggie scum bag" (J.M.T.J.M.P. 14).

Emotion

The domain 'Emotion' in this study refers to a woman's reaction and feelings to monitoring and maintaining her CBG concentrations. Some women felt it was a privilege to have been diagnosed with GDM as it meant they learnt new skills that directed positive lifestyle changes. The sense of achievements in mastering CBG collection and staying within recommended glycaemic targets enabled optimal glucose monitoring. This led to testing family and friends without understanding that this would be recorded on the glucometer as their results.

"It's been a good adjustment, kind of a joy, I learnt how to test blood sugars and I am living healthy, it's kind of like a good stepping stone to continue that healthy life. It's kind of giving you this mirror glass into the future that you could have diabetes in the future (Esther 07B). I'm brave, I never forget to do the pricks" (Raynia 09)

Barriers included emotions of stress and being scared to do the capillary testing at the appropriate times, especially where a needle phobia existed. The constant focus on the numbers discouraged some women from performing regular CBG testing.

"Ah yes, I am scared, first of all 'cause I hate needles. One thing, it should be different that putting like, when we test our diabetes, the needle we put in our fingers, it's very painful, like all my fingers have holes, because every day I prick and then I stop. So, there should be different type of thing we can measure the diabetes" (Shairin 11).

"Um, I guess, having had that experience before as part of my medical training, I kinda knew what it was like [being a doctor], but I think it's the repetitiveness, focusing on numbers and having to do it so many times a day, I mean I wince at the lancet, when it goes off as its getting to the point where it's actually getting, you know, traumatised by the pain that comes from the pricked fingers" (Christina 15A).

Behavioural regulation

'Behavioural regulation' refers to a woman's focus on self-monitoring effectively and planning how to incorporate this into her daily life. Women who decided to have all their testing and documentation equipment in a dedicated bag and leaving it at dedicated place at home indicated how helpful this was to undertake the testing regularly. Sharing their glycaemic target achievements on social media, with overseas GDM Facebook groups, and thinking of the health of their baby were identified as motivators to regulate behaviour.

"You just put yourself into a routine. You just have to, for the baby, and have all your gear in a bag, ready to be used anytime and anywhere" (Sabrina 05).

"Yes, having it all planned helps. Every morning at 10.30 I have 30 minutes' walk. And also after afternoon tea and dinner I have 30 minutes walking. It's very good, and I feel I have more energy" (Casey 01A).

What affects a woman's CBG concentration and how does she maintain optimal glycaemic control with this knowledge?

The themes emerging from the interviews from women with GDM relating to the second research question 'What affects a woman's CBG concentration and how does she maintain optimal CBG control with this knowledge?' were categorised into five of the theoretical domains. These were: Knowledge, Beliefs about consequences, Environmental context and resources, Emotion, and Behavioural regulation (Table 5.5). The domains: Belief about consequences, Environmental context and resources and Behavioural regulation were represented most strongly in the context of this question.

Knowledge

In the context of the second research question the domain 'knowledge' refers to a woman's understanding of what affects her CBG concentrations. Women who knew the differences between carbohydrates, proteins, and fats, could read food labels and understood how exercises affected their blood glucose concentrations were more likely to embrace dietary and exercise changes and continue with regular blood glucose monitoring.

"You just fill it up with other stuff, like veggies, depends on what you eat regularly, it you eat KFC all the time then your buggered" (Danielle 06)

"Yeah, so whenever I do my walking after meal, my blood sugar gets low right away, but if I snuggle in the bed after a meal, the blood sugar is high, that's what I notice" (Belle 19A).

Barriers identified included not knowing how to read food labels or how food intake and activity levels impact on glycaemic control or unable to read the information provided, as it was not in the woman's first language. Two women knew how to increase their subcutaneous insulin, so they could continue eating their favourite sweets and carbohydrates and not be concerned about any behavioural lifestyle changes.

"I don't really understand what these food labels mean. I eat the same stuff anyway, not much use knowing it" (Jisha 04).

"So, I ask them, can I just have some insulin, and they say, "Okay". They give me the long-term insulin and now I can have sweets, but my levels are ok" (Casey 01A).

Table 5.5: Enablers and barriers for women with GDM understanding what effects their CBG concentrations

Domains and Definitions	Enablers	Barriers
Knowledge Refers to a woman's understanding of what affects her CBG concentrations	- understanding the difference between carbohydrates, proteins, and fats - ability to read and comprehend food labels - able to understand how physical activity or inactivity affects their CBG concentrations	- lack of understanding which foods and exercises raise the CBG concentrations - not knowing how to read food labels - knowing how to increase insulin to eat favourite sweets
Belief about consequences Refers to a woman's expectations about what affects her CBG concentration	- eating the same food every day for optimal control - using commercially available, pre-assembled ready for cooking, health food bags for optimal control - hearing other women's stories encourages anticipated regret - regular activities easy to incorporate into daily life and ensures healthy baby	- belief only medication controls CBG concentrations - belief that exercises have no effect on CBG concentrations - belief that physical activity can cause pre- term labour
Environmental context and resources Refers to a woman's access to food, exercise equipment and health professionals	- access to dietitian and group sessions - food diary and discussion - food costs are less (no fast foods) - vegetable garden - recipes on social media - stickers identifying pantry food which are suitable - being organised - appropriate food available when not at home - access to exercise equipment (bicycle, tread mill) - family and children creating motivating resources	- dietetic service unavailable - transport and time issues - not documenting a food diary or not knowing about it - health professionals do not discuss content of food diary - food is more expensive (fruit, special bread) - no ethnic food options included - unavailable professional assessment for exercise or physical activities - easy access to sugary food and drinks
Emotions Refers to a woman's reaction/feelings to what affects her CBG concentrations	- excited to understand the link between food and exercise and CBG concentrations	- stressed about trying hard but not able to achieve optimal CBG concentrations - feeling hungry most of the time
Behavioural regulation Refers to a woman's focus on self-monitoring effective food intake and exercise and planning how to incorporate this into daily life	- self-monitoring with food diary - developing an activity diary - calling exercise physical activity - calling diet food intake, or what to eat - action plan for physical activities - creatively incorporating family exercises - family and children creating resources together	- dislike of exercises - medication and food is enough to maintain CBG concentrations - stress or excitement increases CBG concentrations, too hard to control

Belief about consequences

The 'Belief about consequences' domain refers to a woman's expectations about what affects her CBG concentration. Several women started eating the same food every day. Some women ordered weekly commercially available, pre-assembled ready for cooking, health food bags, as this enabled women to keep their CBG concentrations within the recommended glycaemic targets. While this method of food intake was identified as an enabler by the women, it is unclear how effective long-term lifestyle changes would be sustained, as the women were not planning to eat in a similar way after the baby was born. Further enablers were identified as hearing other women's stories about GDM, which encouraged anticipated regret ('I know if I do this I will regret it, therefore I will not do it'). This meant women were diligent about routinely exercising and following their diabetic diet.

"I focused on it's a short period of time, eating the same every day, you can get through it, and after pregnancy it's going to be so awesome that you can eat what you want to eat, you focus on the fact that it's not forever, I always think of trying to push a baby out that is too big, that's an incentive, they can dislocate if it's too wide, so I just focus on every little bit, makes a difference, that's what I picked up from the obstetrician, you might go "oh this biscuit won't hurt" but yeah it makes a difference, no option but do it consistently. I know of women who so regretted that they did not do it properly" (Annie 16A).

Women in the study who believed that exercises had no effect on CBG concentration were not likely to engage in any physical activity. Women who believed that too much physical activity may cause pre-term labour would do occasionally a short walk. The belief that the diabetes medication would control CBG concentrations prevented women from engaging in understanding the effects of food intake and glycaemic control.

"I've never tested after doing exercise, yeah, so I couldn't say, I don't belief it makes a difference, so don't do it really" (Alice 10A).

"I don't want my baby to come before 35 weeks, you know, I'm scared it comes early, more exercise makes it too early, but I will walk or swim after that time if it makes a difference" (Anna 07).

"I feel better now that I'm on the right medication. My sugars are well controlled and I don't need to worry about eating and walking" (Erin 04B).

Environmental context and resources

In the context of this research question this domain refers to a woman's access to food, exercise equipment and health professionals. Women in this study, who had access to group or individual sessions with a dietitian, could understand and alter their food intake and keep a food diary. Being taught

CBG testing by a pharmacist or by a diabetes midwife in a group session was experienced as an enabler by most women interviewed. Having easy access to exercise equipment, such as a tread-mill or stationary bicycle, enabled women to exercise if they were unable to leave the house. Other enablers were identified as ensuring 'right' food in the pantry, having access to a vegetable garden, lower food costs, less fast food meals, and easy phone access to a diabetes dietitian.

"Walking through a personalised diet is really helpful, and not just a mass-produced 'try these things' and straight access to the dietitian via phone or email. I know what I can and can't eat now. Keeping a food diary has been good" (Anneri 14B).

"I bought a walker machine [treadmill] after being diagnosed with GDM to exercise. Every time I eat I do it. It is working well" (Belle 19A).

Barriers were identified as lack of or limited access to, resources and health professionals. This included lack of access to transport to attend group or individual sessions with a dietitian, no considerations for ethnic food options, not being able to discuss the effects on glycaemic control in the woman's first language, health professionals not looking at the food diary, higher food costs and unclear or no guidance about physical activities/exercises and its effect on CBG concentrations.

"Not sure if some food puts it up, it's possible, if I did a food diary I guess I could look it up, but that's a bit tedious" (Toni 03).

"I didn't read it, because it's easier for him to read in English about what types of food you need to eat, it should be in colour and pictures. He doesn't like to read either, but when you give me a colour picture, these are the things you need to eat a lot, and these are things you need to not eat in colour, that would make a difference, then I would understand" (Zeinab 12A).

"I don't do much exercise because I am working all the time. Don't know how to fit it in. Maybe someone needs sit down with me and show me how and when?" [to exercise] (Fiona 02A).

Emotions

The domain 'Emotion' refers to a woman's reaction and feelings as to what affects her CBG concentrations. Enablers most commonly reported were positive emotions, such as being happy and excited to understand the link between food intake and exercises and glycaemic control. Barriers most commonly reported related to negative emotions, such as being stressed about not seeing any difference in glycaemic control despite trying hard to follow the dietary guidelines and feeling hungry most of the time when trying to achieve optimal glycaemic control.

"There are days when I am so worried that I am eating the wrong food and might hurt my baby, where I have checked myself 12 times just to see where I am staying at because the strict diet does not make a difference [to CBG concentrations], maybe I should just stop altogether? If you don't know, you don't know" (Aroha 10B).

"…but if I'm too hungry then I don't care, which is quite often" (Elizabeth 08B).

"I was kind of worried about what the dietician was going to say because I did have a few highs like in my first week of trying and I remember just feeling so overwhelmed and walking in she said, 'are you OK?' and I just burst into tears, it was just one of those things. She said: "Oh my goodness, I'm not going to tell you off or anything, we'll work through it" (Collette 09B).

Behavioural regulation

The domain 'Behavioural regulation' refers to a woman's focus on self-monitoring effective food intake and exercise and planning how to incorporate this into daily life. Women who had action plans in place for physical activity and food intake, for example to do 20-minute exercise after each main meal, bathing the toddler after the evening meal, playing ball games with the family, and starting a food and activity diary, found it easy to incorporate the changes into their daily life. Renaming exercise as physical activity and diet as food intake made a significant difference for women's confidence level to self-monitor these.

"Oh, you will laugh, but I don't try to vacuum the floor, I brush the floor every night time on my knees with a brush and shovel, because I can't go out and I get cold. My levels are good when I do this. No good levels when I do not do it" (Jisha 04A).

Barriers to changing and regulating behaviour were mainly the dislike of having to exercise or to focus constantly on what to eat. Women noted that both stress and excitement would increase CBG concentrations and this discouraged effective self-monitoring.

"For the baby shower, I was so good with the food but my levels were still high, it's not just stress but also excitement that puts it up. So, what use is that then not to feel happy. May as well not do the testing" (Raman 17B).

What support have women found helpful/not helpful in learning about and maintaining CBG control?

The key themes emerging from the interviews for women with GDM relating to the third research question 'What support have women found helpful/not helpful in learning about and maintaining CBG control?' were categorised into four of the theoretical domains. These are: Beliefs about consequences, Reinforcement, Environmental context and resources and social influences (Table 5.6). The domains

Environmental context and resources and Social influences were represented most strongly in the context of this question.

Beliefs about consequences

The domain 'Beliefs about consequences' refers to a woman's expectation to sharing her diagnosis of GDM with others. Women shared their diagnosis and management of GDM with significant others and work colleagues when they believed this would gain them support for learning more about and maintaining optimal glycaemic control. Interestingly, when women perceived that sharing their diagnosis would generate a judgement and/or unhelpful advice they would not 'tell'. Some women did not 'tell' because they felt protective towards their family members and did not want to worry them unnecessarily. This created a lonely place for some women.

"It helps them to be more supportive if they know. I told them all. I don't want them to bring sugary items when they visit" (Collette 09B).

"Did not tell, as I am big and people will say, ah, yes, you are fat, that did it" (Jean 16B).

"Did not tell parents and friends, as they get too worried, but a bit lonely and hard doing it without them" (Aliisa 02B).

Table 5.6: Enablers and barriers of support for women with GDM about maintaining optimal CBG control

Domains and Definitions	Enablers	Barriers
Beliefs about consequences Refers to a woman's expectation to sharing her diagnosis of GDM with others	- telling others about GDM diagnosis gains valuable support	Not telling others about GDM diagnosis because: - concern for other family members - being judged by family, friends and work colleagues - being told what and what not to eat
Reinforcement Refers to a woman's ability to reinforce skills and coping strategies for self-support in maintaining optimal glycaemic control	- continuing with food diary, feeling better - photos of food eaten instead of written food dairy - self-rewards with non-food items - documenting CBG results - activities connected with family fun	
Environmental context and resources Refers to a woman's ability to have access to learning resources and professional services for optimal glycaemic control	- written information in first language - visual information - informative websites - partner and extended family able to attend teaching or clinic sessions - work colleagues enquiring and providing healthy food options - efficient clinic appointment system - health professional phone support - free health shuttle for appointments - hospital crèche - stickers with healthy GDM messages encourages adherence to healthy food and exercises	- health professional impatient - health professionals inconsistent with advice - not seeing the same health professional twice - long waiting times at clinic - not taught in first language - unable to write the food dairy in first language - no visual information available - website information random and scary - poor parking facilities - no transport available - unable to pay for petrol - no child care support - restaurants unable provide an ingredients list for meals - partner and extended family provide unhealthy meals
Social influences Refers to a woman's access to social interaction to learning/reinforcing optimal glycaemic control	- social media (Facebook) - sharing recipes - group teaching - meeting other women with GDM - partner, family, and friend's interest - work colleagues support	- unsupportive family members and workplaces - no social media groups or support groups in NZ - not knowing anyone with GDM - unable to perform testing in public - told what to eat by family members

Reinforcement

'Reinforcement' here refers to a woman's ability to reinforce skills and coping strategies for self-support in maintaining optimal CBG control. Continuing with a written or creating a pictorial food diary (taking photos with a mobile phone camera), honestly and diligently documenting CBG results and rewarding glycaemic achievements with non-food items or activities (for example, going to the movies) were identified as enabling reinforcement of skills and coping strategies. Family activities such as family members guessing around the dinner table what the CBG concentrations will be before and after the meal, creating a graph for the fridge for charting CBG concentrations for all to view and using stickers to identify in the pantry/fridge which foods are healthy options for women with GDM to consume were further reinforcing enablers.

"It's kind of a fun time. My husband and my daughter guess what the number should be after I have done the pricking. If we are all right we reward us with going to the playground park with my daughter, she loves it and so do we" (BC 17A).

Environmental context and resources

The domain 'Environmental context and resources' refers to a woman's ability to have access to learning resources and health professional services for optimal glycaemic control. Visual information, such as a food plate with portion sizes and access to informative websites about GDM were identified as enablers. Provision of a free health shuttle for clinic appointments, a hospital crèche for child care, an efficient appointment system reducing waiting times and partner and extended family welcomed at teaching sessions and clinic appointments contributed to women's ability to perform CBG testing confidently and of feeling supported. Telephone access to discuss CBG results was available for most women and while only a few women used it, telephone access was considered a reassuring support. Provision of healthy food options by family and work colleagues was reported as a significant support.

"Yeah husband attending info sessions was good but next time not during office time, evenings or weekends would be better. The food plate was very helpful, but maybe more Asian food on it would help too" (Amali 16).

Several women had experienced barriers to accessing learning resources and health professional services for optimal glycaemic control. These included health professionals being impatient and inconsistent in their advice; not seeing the same health professional twice; not being taught how to check the glucometer; long waiting times at clinic appointments; not being taught in their first language, being unable to write into their food diaries in their first language; having no transport to attend teaching

sessions or clinic appointments and poor parking facilities. Of the women who searched for information through Google, some became scared and would have preferred guidance to visit a website with clear and supportive information. Restaurants being unable to provide an ingredients list for meals on the menu was identified as another inaccessible resource. Provision of unhealthy food by family and work colleagues was reported as a significant barrier.

"Google was a bit scary. So, it's better just to stay away from it and get your questions answered at the clinic. But that google information was in Russian, and that was good. Yeah, they need to tell me where to look on the internet. Same with menus from restaurants, their ingredients could be listed on-line" (Lilly 18A).

"I saw a registrar who seemed very junior and gave me quite conflicting information to what everybody else had given me. So, I actually went back yesterday and saw a consultant, because I wasn't happy. That improved things, but it took more time and to find a carpark is nearly impossible" (Erin 18B).

"He says, "Just eat whatever you want", because he likes sweet stuff". Hard not to give in" (Tara 19B).

Social influences

The domain 'Social influences' refers to a woman's access to social interaction to learning/reinforcing optimal blood glucose control. Some women joined an American Facebook group for women with GDM. While the glycaemic targets were different for the American counterparts, women in this study enjoyed swapping recipes, sharing tips about CBG testing, celebrating successes of achieving and maintaining glycaemic control and providing encouragement when glycaemic challenges were shared. Family and friend's interest in all aspect of glycaemic control and meeting other women with GDM contributed to feeling supported and reinforcement for optimal glycaemic control.

"So, I soon realised, after joining a [American] Facebook group, that most people struggle with cereals. So, I removed the cereal and just went to a two-egg breakfast, and that just evened it out. So, then I felt a bit better again" (Anneri 14B).

"Yes, in the morning, if I want to sleep in then he will do for me the fingerpicks" (Shairin 11).

Participating women identified social disconnections as barriers for learning and reinforcing optimal glycaemic control. This included unsupportive family members and workplaces, unavailability of a support group for women with GDM in New Zealand, on-line or face-to-face, being judged in public and being constantly' told what to eat and what not to eat by family members.

"…I guess that's why I eat my chocolate with my yoghurt. I like chocolate, I'm going to have chocolate. You tell me I can't, then I'm not going to listen. And I'm going to want it more and I'm going to binge eat it and don't worry about my levels" (Aroha 10B).

The results from the three questions explored in this study identified enablers and barriers for women with GDM representing their experiences of monitoring CBG concentrations, what affects this monitoring and what supports have been helpful for them to achieve optimal glycaemic control. As a summary, Table 5.7 outlines some considerations for practice and research that may be useful for health professionals and diabetes in pregnancy services providing care for women with GDM.

Table 5.7: Considerations for practice and research

Practice considerations	Research considerations
Monitoring for optimal glycaemic control	**Monitoring for optimal glycaemic control**
• Enable women with GDM to attend group teaching for CBG testing and interpretation, and include women who have had GDM to share their stories. • Discuss individual strategies for regular CBG monitoring, food intake and physical activity. • Encourage partner and family attendance at any clinic or teaching sessions (may need to be offered at evenings or weekends). • Provide information relating to GDM in a woman's first language and/or more visually, including ethnic food suggestions. • Investigate the possibility of community pharmacists' involvement in teaching CBG testing.	• Explore opportunities for companies to create phone Apps, e.g. for electronic food and activity diaries, recording of CBG results and medication intake. • Do phone apps have an impact on optimal glycaemic control for women with GDM? • Does a name change for GDM reduce anxiety in pregnant women?
Dietary intake and exercise for glycaemic control	**Dietary intake and exercise for glycaemic control**
• Enable easy access to a diabetes dietitian with diet recommendations tailored to an individual woman's context (cultural, financial, and emotional). • Engage in meaningful discussions about the content in a food diary and provide multi-modal opportunity for the woman to record the food diary in her first language or enable mobile phone photo collection of food intake. • Regularly address hunger for women with GDM. • Encourage a physical activity diary alongside the food diary. • Consider engaging a physical therapist for clear in-depth assessment and guidance of exercise that women can incorporate into their daily life.	• Does keeping a physical activity diary impact on glycaemic control? • Does engaging a physical activity therapist contributes to the understanding and up-take of physical activity for women with GDM? • Why do women with GDM seem to be hungry despite quality dietary recommendations? • What affect has self-imposed dietary practices by women with GDM during their pregnancy on long term lifestyle behaviour?
Support for optimal glycaemic control	**Support for optimal glycaemic control**
• Provide free CBG monitoring equipment, health shuttles and child care when attending clinic appointments and reduce clinic waiting times. • Consider face-to-face support groups for women with GDM. • Consider setting up a social media group for women. with current GDM (e.g. Facebook). • Include regular mental health assessment for women with GDM. • Provide direct phone access to multi-disciplinary health professionals.	• Limited research available for regular mental health assessment for women with GDM. • Limited research about the effect of a GDM diagnosis on partners and family members. • Limited research on how partners and families can best support a woman with GDM in their context. • Does social media or face-face group support make a difference for women with GDM for maintaining optimal glycaemic control?

5.2.4 Discussion

Our results highlight the complex interactions between women with GDM monitoring their CBG concentrations, their understanding of the link between dietary intake, exercise and glycaemic control, having stress-free access to health care providers and resources, and their social context and support. The study used interviews and the validated TDF to determine the enablers and barriers women with GDM experience to achieve optimal CBG control. We categorised emerging enablers and barriers into a total of nine domains across three study questions. These were: Knowledge, Skills, Beliefs about capabilities, Beliefs about consequences, Reinforcement, Memory, attention and decision processes, Environmental context and resources, Social influences, Emotion and Behaviour regulation (Table 5.4 to 5.6). Through our iterative process we identified when no new themes were emerging within the TDF domains, thus ensuring that data saturation had been achieved (Sanders 2010; Wright 2011). Transcript analysis revealed a range of enablers and barriers that impact on a woman's ability to achieve optimal glycaemic control.

The initial response of women being diagnosed with GDM was predominantly of being shocked. At the time of the interview the women had generally accepted the diagnosis, knowing it would only last a finite time and were motivated by making a difference for the baby. Maternal shock, fear and anxiety associated with a diagnosis of GDM have been reported in the literature with a trend towards acceptance as the pregnancy progressed (Persson 2010; Collier 2011; Hirst 2012; Morrison 2014; Parsons 2014; Kaptein 2015). Kalra and colleagues (2013) suggest that these findings support an onomastic (re-naming) opportunity, arguing that the phrase gestational diabetes can cause significant psychosocial morbidity. Alternative names suggested for GDM were Gestational Dysglycemia of Nutritional Origin (GDNO) or Pregnancy Related Intolerance to Glucose (PRIG). This indicates further research is needed to determine if an onomastic change would achieve less maternal psychosocial morbidity. Some women in our study, once they overcame the initial shock, thought that it was a 'privilege 'and a 'good thing' to have been diagnosed with GDM, as this supported change to a healthier lifestyle and provided them with skills such as being able to read and understand food labels. This advocates for an opportunity for promoting lasting lifestyle changes during the remainder of the pregnancy. Other studies reiterate these findings, and found that for some women with GDM, the knowledge gained enhanced the motivation and self-efficacy to initiate lasting lifestyle changes (Evans 2005; Devsam 2013; Morrison 2014).

While most women accepted that they had GDM and adapted to the change, many women disliked the change of focus for their pregnancy to numbers of CBG concentrations, glycaemic targets, 90th percentile for fetal growth and maternal weight. This contributed to a feeling of reduced control, which exacerbated emotions and created barriers for some women. This meant a few women in the study did not continue with or reduced their self-monitoring of CBG concentrations, decided they were too busy to attend some of the clinic appointments, refused referrals for serial growth scans and were less committed to adhere to diet recommendations. Negative feelings acting as a deterrent to intervention up-take has been reported for women with GDM by some studies (Razee 2010; Parsons 2014; Carolan-Olah 2016). This suggests that emotional support and mental health assessments need to be an imperative part of heath care for women with GDM.

Monitoring for optimal glycaemic control

Nearly all women in our study knew their optimal glycaemic targets and the importance to adhere to them. Despite this knowledge, participating women reported that this did not necessarily mean they would self-monitor their glycaemic control as advised. Responses varied on how they felt about their self-monitoring skills, if they had access to equipment, and their context, evident through the most strongly represented domains of Belief about capabilities, Emotions and Social influences. Women were less likely to do the CBG testing or stopped altogether for a variety of reasons. These included being scared and unsure about pricking their finger for CBG testing, playing a musical instrument, believing high CBG concentrations would harm their baby, being asked to leave a restaurant when testing, not being able to take a break to perform the test because of the nature of their work, and not being believed that their recorded CBG results were correct. Women were more likely to continue with regular CBG testing if they thought it was less painful than anticipated, attended a group session to learn how to perform CBG testing, took family members to teaching sessions, were shown by a community pharmacist how do to the testing, had the belief they knew how to do it, were praised by health professionals for their efforts, and had fun ‘pricking’ friends and family. There is a need for health professionals to provide clear and meaningful information about CBG testing, discuss strategies for overcoming barriers particularly in work situations, enable family members to be part of this process and to believe a woman’s CBG recordings (Table 5.7). These findings are echoed in other literature (Carolan 2012b; Parsons 2014). The notion for a community pharmacist to initially teach women diagnosed with GDM how to perform CBG testing may be a valuable option to consider when time, cost and distance are a barrier. Some studies involving patients (pre-diabetic or with T2DM) self-monitoring their CBG

concentration have found community pharmacies specialised in diabetes care can provide this service effectively (Müller 2006; Mansell 2016). An extensive literature search did not identify any studies involving women with GDM and the effects of being taught CBG testing by a local community pharmacist. Clearly this is an area where further research is required (Table 5.7).

Dietary intake and exercise for optimal glycaemic control

Our study demonstrated that the domains Belief about consequences, Environmental context and resources and Behavioural regulation were represented most strongly in the context of dietary intake and exercise for enabler and barrier identification. Studies have reported that women with GDM who were treated with dietary advice and were self-monitoring CBG concentrations had fewer macrosomic babies, less maternal weight gain and less birth trauma (Crowther 2005; Hawkins 2009).

A Cochrane systematic review assessed evidence from 19 trials for ten different dietary interventions and concluded that while dietary advice is the main strategy for managing GDM it remains unclear which type of diet is best (Han 2017). Dietary self-management guided by CBG concentrations alone without a particular diet may be difficult for women with GDM. In our study, participants who understood the benefits and consequences of dietary self-management and regular exercise for controlling their CBG concentrations had access to professional dietetic advice and could incorporate effective physical activities into their daily life achieved optimal glycaemic control most of the time. This is consistent with other studies (Persson 2010; Carolan 2012b; Hui 2014; Wang 2016).

Women in our study saw self-imposed dietary restrictions such as eating the same meal every day or ordering commercially pre-packed health food options as enablers, and for them these were solutions to their current hyperglycaemia, as GDM was understood to be transitory. This self-imposed practice resulted in a woman's CBG concentrations staying within her recommended glycaemic targets most of the time. It is questionable if this approach would achieve long-term lifestyle changes. It is possible that the women in our study may not have understood the link between GDM and the risk for subsequent development of T2DM, and the importance of health behaviour regulation for reducing future diabetes risk (Kapur 2008; Balas-Nakash 2010; Hirst 2012). Health professionals need to ascertain from women the reasons for any self-imposed dietary practices and ensure future health implications are understood. Further research is needed to explore in depth if self-imposed dietary practices by women with GDM during their pregnancy affect long term lifestyle behaviour (Table 5.7).

Over half of the women in this study identified a barrier to written information, as it was only provided in English. They wanted the health information in either their first language or for it to be more visually presented to better understand their GDM diagnosis, what optimal blood glucose control meant and to include ethnic food options (Table 5.7). These are similar findings reported by qualitative studies for women with GDM in Vietnam (Hirst 2012), Italy (Lapolla 2012) and South Tamil Nadu (Bhavadharini 2017). Women in our study identified Google as a helpful tool, especially if they could access websites in their first language through Google. Health professionals need to be aware that women will access information beyond the clinic environment and that the quality of this information may vary. Health literacy providing clear and relevant health messages for women with GDM or other types of diabetes has been identified as an effective way to help people manage their own health care (Al Sayah 2013; Work Base Education Trust 2014; Hussain 2015; Ministry of Health 2015a).

Most women commented on being hungry, but felt they could endure this for their babies' health, if it kept their CBG concentrations within the recommended glycaemic targets. Dietetic advice needs to include how to address hunger for women with GDM (Table 5.7).

Regular aerobic exercises involving large muscle groups such as walking, swimming and stationary cycling have been reported to be beneficial in pregnancy and are not associated with harms to the baby (ACOG 2015; Russo 2015). The prevalence of exercise for women with GDM during their pregnancy appeared to be related to their understanding of what type of exercise they could do and its duration. This was further compounded by their inability to incorporate exercises into their busy daily life and the fact that it was called exercise. The lack of specific recommendation on type, intensity, and duration of exercises from health professionals and women's beliefs that exercises could cause pre-term labour or that rest is required when pregnant has been reported in the literature (Mudd 2013; Carolan-OIah 2016; Momeni 2016; Wang 2016).

Participating women, who approached exercises as meaning to be physical activity, were more likely to think outside the (exercise) square, and welcomed discovering which physical activity, such as bathing the toddler after the evening meal, had an impact on their glycaemic control.

A Cochrane systematic review on exercise for pregnant women with GDM for improving maternal and fetal outcomes summarised evidence from 11 randomised controlled trials and found while exercises appeared to lower fasting and post-prandial CBG concentrations, they did not find any differences in

other outcomes for pregnant women with GDM (Brown 2017). However, even if exercise does not provide any benefit during pregnancy, this change in lifestyle may persist after birth, and may help prevent the onset of type 2 diabetes and its long-term complications. A prospective study of 4554 women with previous GDM, who were followed for 16 years showed that increased physical activity levels lowered T2DM development and its risks (Bao 2014).

This may mean that for women with GDM it could be worthwhile to record physical activities alongside or as part of their food diary for them to understand the effect physical activities have on their CBG concentrations (Table 5.7). It is common practice for the dietitian or the Lead Maternity Carer (LMC) midwife to recommended daily walking but without further in-depth guidance. Meeting with a physical activity professional or therapist who assesses where and what physical activities could be adapted to a woman's daily context, alongside other health professionals at the diabetes in pregnancy clinic, may be an option to consider and would benefit from further research (Table 5.7).

Support for glycaemic optimal control

Women reported that support from partners, family, friends, work colleagues and health professionals made a significant difference for them to accept their diagnosis, adhere to prescribed treatment and maintain optimal glycaemic control. This support facilitated self-management and healthy lifestyle behaviours. Partners and extended family support was reported as valuable in particular for increasing exercise and the provision of healthy meals. Similar findings have been reported in the literature (Carolan 2012b; Devsam 2013; Parsons 2014; Kaptein 2015). The key domains identified for this section of social influences and belief about consequences reflect this. Other suggestions for support included joining a social media network for women with current GDM, for example on Facebook, and/or attend a local support group for women with GDM. Neither of these are currently available in New Zealand and support organisations for Diabetes or DHB's may want to consider this (Table 5.7).

Some women in this study found their family's excessive concerns or providing unhealthy meals a challenge and reported that this contributed to them feeling stressed and unable to perform CBG monitoring. A qualitative study of perceived needs in women with GDM found similar findings and indicates the importance for health professionals to increase their awareness for the need of social support for women with GDM (Khooshehchin 2016). Other studies including women with borderline GDM and T2DM reiterate this (Mayberry 2012; Miller 2013; Greenhalgh 2015; Han 2017) and recommend, that health professionals as part of clinic appointments need to include discussions about

effective strategies to cope with situations that are challenging for women with GDM. Research about the effect of a GDM diagnosis on partners and family members and how they can best support a woman with GDM in their context is limited (Table 5.7). Complexities of social determinants of health is often studied with ethnographic research (Bandyopadhya 2011b) and it may be appropriate to encourage this type of research for partner and family experience who are living and supporting women with GDM.

Within the identified key domain of belief about consequences, a surprise finding was that several women reported not sharing their GDM diagnosis with anyone other than their partners. The main reasons for this decision was fear of being judged, not wanting to be scrutinised for daily activities including food intake, or not wanting to worry extended family members. This created social isolation, and contributed to a woman's feeling of shame, guilt, and reduced her ability to achieve optimal glycaemic control. Qualitative studies support these findings (Abdoli 2012; Collier 2011; Ghaffari 2014; Schabert 2013). The women in our study had not shared this decision with their respective health professionals. This suggests the need for greater awareness among health professionals that some women with GDM 'do not tell' and on-going assessment of a woman's mental well-being should be included in the health services provision (Morrison 2014).

This study adds to the body of knowledge about enabling women with GDM to achieve optimal glycaemic control. While some studies have explored the GDM experience from the woman's point of view, none have specifically studied the enablers and barriers to achieving optimal glycaemic control using the validated Theoretical Domains Framework. The sample size was reflective of a cross section of the demographics of New Zealand's pregnant population and reached data saturation.

Limitations of our study were that participating women were not from rural or remote areas in New Zealand and only women who were fluent in English were eligible. Women from different cultural backgrounds were well represented in this study (Table 5.3). It is unclear if the interviews with women in their first language would have elicited different enablers and barriers for optimal glycaemic control. Women interviewed often asked for information in their first language. Future research should consider conducting interviews in a participant's first language.

5.2.5 Conclusions

This qualitative study has identified enablers and barriers for women with GDM to achieve optimal glycaemic control providing insights as to how women accept a diagnosis of GDM, adapt to regular CBG self-monitoring, adhere to recommended treatments, undertake necessary lifestyle changes and can be supported. The enablers and barriers identified are multidimensional and may assist health professionals and diabetes in pregnancy services on how best to meet the needs of this diverse group of women and their families to achieve optimal CBG control and so reduce adverse outcomes for women with GDM and their babies.

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Availability of data and materials

The interview guide, study protocol and dataset supporting the conclusions of this article is held by the authors. The de-identified data may be made available on request.

Authors' contributions

Ruth Martis (RM) designed the qualitative study, recruited the women, conducted the interviews, led the analysis, prepared the first draft of the manuscript and subsequent drafts. RM and Julie Brown (JB) coded and classified the data, revised and synthesised text into final domains and consulted with the other authors Caroline Crowther (CAC) and Judith McAra-Couper (JMC) during the process. CAC and JB contributed to the study design, project administration, thematic interpretation, and commented on drafts of the manuscript. All authors read and approved the final version.

Competing interests

None of the authors have any financial conflict of interests associated with this publication. CAC and JB are lead investigators for the TARGET Trial.

Consent for publication

Not applicable

Ethical approval and consent to participate

This qualitative study was nested within the TARGET Trial (a stepped wedge randomised controlled trial (Australian New Zealand Trial Registry: ACTRN12615000282583)) and approved by the New Zealand Health and Disability Ethics committee (HDEC) Ref. 14/NTA/163, research registration number 1965. Locality agreements were obtained from Canterbury and Counties Manukau District Health Boards. Eligible women who wished to participate signed a consent form for this study.

Chapter 6: Summary conclusion

This thesis aimed to address the research gaps identified after reviewing the literature on treatments and experiences for women with GDM. The gaps highlighted the need to synthesise the evidence from systematic reviews on treatments for women with GDM and from randomised controlled trials of glycaemic treatment targets for women with GDM, as well as the need to investigate women's views and experiences, barriers, and enablers for improving health outcomes. In this chapter, the key findings from each study will be summarised and the implications for clinical practice and further research identified presented.

6.1 Research question 1: Which treatments are effective for women with GDM?

6.1.1 Aim: To synthesise the current research evidence of Cochrane systematic reviews on treatments for women with GDM and to identify specific research gaps of treatments for women with GDM requiring further primary research.

A comprehensive overview of existing Cochrane systematic reviews on treatments for women with GDM was prepared, summarising the available evidence on the effectiveness of treatments for women with GDM and their infants. This included quality assessments for the included studies and the pre-specified primary and secondary outcomes. The Overview was entitled: **Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews.** It is hoped that the Overview can be used as a one-stop resource to inform health professionals, consumers, clinical guideline developers, health policy makers and researchers.

Summary of findings

The Overview included eight Cochrane systematic reviews that reported on 62 randomised trials that included 9133 women, 8373 babies and 767 children. All the included systematic reviews were of high-quality and of low-risk of bias (AMSTAR and ROBIS).

The quality of the evidence from the randomised trials included in the eligible systematic reviews ranged from high- to very low-quality (GRADE) with most of the included trials being assessed as low- to very low-quality. Data were available from the included reviews for 59 (74%) pre-specified overview outcomes of the 80 listed in the protocol for this Overview.

Findings from high-quality evidence in the Overview suggest that lifestyle interventions are ineffective for reducing the likelihood of induction of labour compared with usual diet/diet alone and that exercise

compared with control is ineffective in improving the return to pre-pregnancy weight. No other high-quality evidence was found.

The available moderate-quality evidence does suggest some promising interventions for which more high-quality evidence is needed: Lifestyle interventions (reduced risk of LGA) and the DASH diet (reduced rate of caesarean section). Lifestyle interventions and considering the DASH diet may be useful for some women with GDM as treatment interventions with or without additional pharmacotherapy alongside appropriate advice and/or supervision from a health professional (Table 6.1). Long-term health outcomes for women and their infants and costs have not been well reported (Table 6.1).

Implications for clinical practice from the Overview findings

Lifestyle interventions, that include advice on diet and physical activity, have become the mainstay of treatment for women with GDM and are recommended in many national clinical practice guidelines. However, many of the lifestyle and exercise interventions are multi-component and identifying which of the individual components are effective or not effective is impossible with the currently available evidence reported in the Overview.

Most dietary treatments assessed in this Overview are from interventions reported as single studies, often with a small number of participants, and only a few trials have compared the same or similar dietary interventions. Therefore, there is limited high-quality evidence about the effects on health outcomes of relevance for women with GDM and their babies to guide or inform clinical practice (Table 6.1).

Considerations for future research from the Overview

This Overview highlights that there is limited evidence to make conclusions on the effects on relevant health outcomes for many current treatments for women with GDM. Further high-quality research is required to identify the most effective components or combination of components for the lifestyle and exercise interventions (Table 6.1).

Other dietary interventions may be beneficial, but any effect is currently difficult to identify because of multiple comparisons, small sample sizes and the limited quantity and quality of trials.

Further large high-quality studies with appropriate sample sizes are required, particularly for the DASH diet, to assess their effectiveness for improving short-and long-term maternal and infant outcomes and to assess the costs for treatments, family and services (Table 6.1).

6.2 Research question 2: Which glycaemic treatment targets best benefit the health of women diagnosed with GDM and their babies?

6.2.1 Aim: To synthesise and assess the current research evidence from randomised controlled trials on the effect of different glycaemic targets for women with GDM and their children and to identify specific research gaps of glycaemic targets to guide treatment for women with GDM requiring further primary research.

A Cochrane systematic review entitled: **Different intensities of glycaemic control for women with gestational diabetes mellitus** was prepared, following production of a systematic review protocol that was peer reviewed, and published in the Cochrane Library (Martis 2016a). The systematic review assessed the available evidence from randomised controlled trials on the effect of different treatment targets for glycaemic control in pregnant women with GDM on maternal and infant health outcomes.

Summary of the Cochrane systematic review findings

Only one randomised controlled trial, involving 180 women, was identified that met the inclusion criteria for this systematic review. In this trial, the capillary glycaemic targets compared were: pre-prandial: 5.0 mmol/L (90 mg/dL) and at one-hour postprandial: 6.7 mmol/L (120 mg/dL) for the *strict* group and for the *liberal* glycaemic group: pre-prandial 5.8 mmol/L (104 mg/dL) and at one-hour postprandial 7.8 mmol/L (140 mg/dL).

The included trial did not report on any of the systematic review's primary outcomes but did report data relating to some of the maternal and infant secondary outcomes. For the use of pharmacological therapy, a maternal secondary outcome, the *strict* glycaemic targets were associated with a non-significant increase in the use of insulin requirements (33/85; 39%) compared with *liberal* glycaemic targets (18/86; 21%) (RR 1.85, 95% CI 1.14 to 3.03; one trial, 171 women). The confidence intervals are wide suggesting imprecision and caution is required when interpreting the data. No clear differences were seen for any of the other secondary outcomes, including long-term outcomes. Based on the current limited data it remains unclear which glycaemic targets should be recommended for women with GDM for improving their health and the health of their babies.

Implications for clinical practice the Cochrane systematic review

There was non-significant evidence that women using *stricter* glycaemic targets in the included study used more insulin therapy. No data were provided for adverse effects such as maternal hypoglycaemia. There was no difference in the risk of the infant being born small-for-gestational age. There is currently

insufficient evidence to support *stricter* over more *liberal* glycaemic treatment targets for women with GDM for guiding clinical practice (Table 6.1). Although the current available evidence provides limited guidance for clinical practice, four ongoing randomised controlled trials have been identified and data from these studies will increase the knowledge base and once published will be included in future updates of this systematic review.

Considerations for future research the Cochrane systematic review

This systematic review highlights the need for further larger, high-quality trials that compare different intensities of glycaemic control targets to guide the treatment of women with GDM. High-quality trials should evaluate different glycaemic targets to guide treatment for GDM and assess both short- and long-term health outcomes for mothers and their infants including health costs for services and women with GDM. It is also important to evaluate women's views of adhering to different glycaemic intensities and how this affects their daily life to understand and overcome impracticalities and inconveniences such as hospital clinic attendances, and the effects of capillary blood glucose monitoring, as well as financial costs (Table 6.1).

6.3 Research question 3: What do women with GDM say are the barriers and enablers for their glycaemic targets?

6.3.1 Aim: To investigate how women with GDM view their glycaemic treatment targets and identify the barriers and enablers for them in achieving optimal glycaemic control using a quantitative research approach.

This published quantitative study reports the results of a face-to-face and telephone survey administered to 60 women diagnosed with GDM at two distinct different geographic locations in New Zealand to investigate existing barriers and enablers to achieving optimal capillary blood glucose control.

Summary of findings of this survey

The majority of women correctly identified their glycaemic treatment targets (59, 98%) and viewed it as very important or important to try to adhere to these targets. Documenting the blood glucose results were viewed as less important (56, 93%) by the women compared to viewing adherence to the targets because women knew the results could be downloaded from the glucometer. These findings were similar across participants regardless of their glycaemic treatment targets.

Nine barriers and ten enablers were identified. Almost two thirds of women found it difficult to achieve adequate morning fasting capillary blood glucose control, regardless of their recommended glycaemic targets, and identified the need for better strategies and adequate health professional and family support to manage this difficulty. Barriers for health information and literacy identified that health professionals need to consider using a women-centred and adult learning style approach, provide visual aids, provide written information in relevant languages, and include extended family members when imparting knowledge or teaching GDM related skills. Long clinic waiting hours, inconsistent advice, judgmental attitudes and not being believed by health professionals requires further consideration when providing a health care service for women with GDM.

Implications for clinical practice from this survey

A wide range of barriers and enablers were reported. The findings from this survey will be useful for developing strategies within Diabetes in Pregnancy Services to better support women with GDM achieve their glycaemic control. Diabetes in Pregnancy Services and health professionals may wish to consider offering group teaching sessions for women with GDM, providing more GDM information with visual aids, providing written information in relevant first languages, and including extended family members when imparting knowledge or teaching GDM related skills (Table 6.1).

Considerations for future research from this survey

We found no published studies that reported on the effects of providing visual learning aids for women with GDM or the impact of having the information about GDM in their first language (Table 6.1). Further research should support the development of effective GDM resources for women with GDM. New Zealand based social media, as in Facebook, was identified as another potential virtual community support by the women surveyed, as this is currently not available. Research into setting up a New Zealand virtual community support group and its effectiveness for women with GDM needs to be considered (Table 6.1). Two thirds of women reported being hungry. It is unclear from the survey if this relates to women trying to lower their morning fasting capillary blood glucose by eating less at dinner-time or eating very low carbohydrate meals. This would benefit from further research to explore and then guide how to overcome this identified barrier (Table 6.1).

6.4 Research question 4: What are women's experiences, barriers, and enablers with their glycaemic targets from a qualitative perspective?

6.4.1 Aim: To examine behavioural factors impacting on women with GDM in achieving optimal glycaemic control.

This qualitative study through semi-structured interviews was conducted with 60 women diagnosed with GDM who had a least two weeks' experience with CBG testing. Using the TDF framework for analysis the results identified existing behavioural factors for women with GDM in achieving optimal glycaemic control.

Summary of findings from the semi-structured interviews

Women reported a shift from their initial negative response of the diagnosis of GDM to accepting their diagnosis but disliked the constant focus on numbers. Barriers and enablers were categorised into 10 theoretical domains across three main areas. The areas comprised:

1. Monitoring for optimal glycaemic control
2. Dietary intake and exercise for optimal glycaemic control
3. Support for optimal glycaemic control

Barriers included: lack of health information, teaching sessions, consultations, and food diaries in a woman's first language; long waiting times at clinic appointments; seeing a different health professional every clinic visit; inconsistent advice; no tailored physical activities assessments; not knowing where to access appropriate information on the internet; unsupportive partners, families, and workplaces; and unavailability of social media or support groups for women with GDM. Perceived judgement by others led some women only to share their GDM diagnosis with their partners. This created social isolation.

Enablers included: the ability to attend group teaching sessions with family and hear from women who have had GDM; easy access to a diabetes dietitian with diet recommendations tailored to a woman's context including ethnic food and financial considerations; free CBG monitoring equipment, health shuttles to take women to appointments; child care when attending clinic appointments; and being taught CBG testing by a community pharmacist.

1. Monitoring for optimal glycaemic control: Implications for clinical practice from the semi-structured interviews

There is a need for health professionals to provide clear and meaningful information about CBG testing, discuss strategies for overcoming barriers particularly in work situations, enable family members to be part of this process and to believe a woman's CBG recordings (Table 6.1). Providing information relating to GDM in a woman's first language and/or more visually, including ethnic food suggestions may increase adherence to glycaemic targets and regular CBG monitoring (Table 6.1). The notion for a community pharmacist to initially teach women diagnosed with GDM how to perform CBG testing may be a valuable option to consider in clinical practice when time, cost and distance are a barrier (Table 6.1).

1. Monitoring for optimal glycaemic control: Considerations for future research from the semi-structured interviews

Women repeatedly asked for easier ways of recording their CBG concentration results or food diary entries. Further research should include exploring opportunities for companies to create phone Apps for electronic food and activity diaries, recording of CBG results and medication intake and assess its effectiveness for monitoring effective glycaemic control (Table 6.1). Some literature suggest that women's anxiety increases after being diagnosed with GDM because of their own and societal connotations attached to the term GDM and have suggested a name change. Alternative names suggested for GDM were Gestational Dysglycemia of Nutritional Origin (GDNO) or Pregnancy Related Intolerance to Glucose (PRIG). Further research is needed exploring if a name change for GDM does reduce anxiety in pregnant women diagnosed with GDM (Table 6.1). Some women in the study were taught CBG testing by their community pharmacists and had reported this to be a positive experience. No research has been published for women with GDM in this area that we could find. Research considerations could include exploring the experiences for women newly diagnosed with GDM being taught by a community pharmacist, and its time and costs effectiveness (Table 6.1).

2. Dietary intake and exercise for optimal glycaemic control: Implications for clinical practice from the semi-structured interviews

Health professionals need to seek from women the reasons for any self-imposed dietary practices and ensure potential future health implications are understood (Table 6.1). Health professionals need to be aware that women will access information beyond the clinic environment, that the quality of this information may vary and that there is a need for guidance to trustworthy internet sites or web pages

Table 6.1: Considerations for clinical practice and research

Clinical practice considerations	Research considerations
Treatments for women with GDM	**Treatments for women with GDM**
• Consider lifestyle interventions for reducing the risk of LGA, promising evidence • Consider exercise for reducing death and serious infant morbidity; promising evidence • Consider the DASH diet for reducing caesarean section rate; promising evidence	• High-quality trials needed for the effective components or combinations of lifestyle interventions • High-quality trials needed for the effective components or combinations of exercise interventions • Further high-quality trials needed with appropriate sample size for the DASH diet to confirm effectiveness for improving short and long-term outcomes • Other dietary interventions need exploring as currently only small size dietary trials available with multiple comparisons; too difficult to identify any benefits • Cost for treatments, family and service requires sufficient powered trials • Long-term outcomes for women with GDM and their children need to be included in any research • Women's experiences of the treatment require further research
Glycaemic targets for women with GDM	**Glycaemic targets for women with GDM**
• Insufficient evidence to recommend stricter or more liberal glycaemic targets for women with GDM; consensus-based recommendations for glycaemic targets	• Large high-quality trials needed to compare different intensities of glycaemic control targets including short and long-term outcomes • Women's experiences with glycaemic targets requires further research • Explore differences and similarities between survey and semi-structured interview method in identifying barriers and enablers for women with GDM and their different glycaemic targets or if a mixed method design is more effective
Monitoring for optimal glycaemic control	**Monitoring for optimal glycaemic control**
• Enable women with GDM to attend group teaching for CBG testing and interpretation, and include women who have had GDM to share their stories. • Discuss individual strategies for regular CBG monitoring, food intake and physical activity. • Encourage partner and family attendance at any clinic or teaching sessions (may need to be offered at evenings or weekends).	• Explore opportunities for companies to create phone Apps, e.g. for electronic food and activity diaries, recording of CBG results and medication intake. • Do phone apps have an impact on optimal glycaemic control for women with GDM? • Does a name change for GDM reduce anxiety in pregnant women? • How effective are visual learning aids for women with GDM? • How effective is having information or clinic appointments in a woman's first language?

Clinical practice considerations	Research considerations
• Provide information relating to GDM in a woman's first language and/or more visually, including ethnic food suggestions and food label reading skills. • Investigate the possibility of community pharmacists' involvement in teaching CBG testing.	
Dietary intake and exercise for glycaemic control	**Dietary intake and exercise for glycaemic control**
• Enable easy access to a diabetes dietitian with diet recommendations tailored to an individual woman's context (cultural, financial, and emotional). • Engage in meaningful discussions about the content in a food diary and provide multi-modal opportunity for the woman to record the food diary in her first language or enable mobile phone photo collection of food intake. • Regularly address hunger for women with GDM. • Encourage a physical activity diary alongside the food diary. • Consider engaging a physical therapist for clear in-depth assessment and guidance of exercise that women can incorporate into their daily life.	• Does keeping a physical activity diary impact on glycaemic control? • Does engaging a physical activity therapist contributes to the understanding and up-take of physical activity for women with GDM? • Why do women with GDM seem to be hungry despite quality dietary recommendations? • What affect has self-imposed dietary practices by women with GDM during their pregnancy on long term lifestyle behaviour?
Support for optimal glycaemic control	**Support for optimal glycaemic control**
• Provide free CBG monitoring equipment, health shuttles and child care when attending clinic appointments and reduce clinic waiting times. • Consider face-to-face support groups for women with GDM. • Consider setting up a social media group for women. with current GDM (e.g. Facebook). • Include regular mental health assessment for women with GDM. • Provide direct phone access to multi-disciplinary health professionals.	• Limited research available for regular mental health assessment for women with GDM. • Limited research about the effect of a GDM diagnosis on partners and family members. • Limited research on how partners and families can best support a woman with GDM in their context. • Cost-effective analysis for free CBG equipment, free health shuttle and free child care for attending clinic appointments • Does face-face group support make a difference for women with GDM for maintaining optimal glycaemic control? • How effective is creating a virtual community support group (social media e.g. Facebook) for women with GDM?

(Table 6.1). Dietetic advice needs to include how to read food labels and address hunger for women with GDM (Table 6.1). Meeting with a physical activity professional or therapist who assesses where and what physical activities could be adapted to a woman's daily context, alongside other health professionals at the diabetes in pregnancy clinic may be a valuable consideration for clinical practice (Table 6.1).

2. Dietary intake and exercise for optimal glycaemic control: Considerations for future research from the semi-structured interviews

The study identified that little information and assessments were provided to participants regarding exercise/physical activity. Further research in this area could clarify its effectiveness including if keeping a physical activity diary, engaging a physical activity therapist and family activity involvement makes a difference for optimal glycaemic control (Table 6.1). Women indicated being hungry most of the time. There is a need for further research to investigate why women with GDM seem to be hungry despite receiving quality dietary recommendations (Table 6.1). Some women ate the same food every day to achieve optimal glycaemic control. It is unclear if this self-imposed practice is beneficial for short term and long-term lifestyle behaviour and would benefit from further research (Table 6.1).

3. Support for optimal glycaemic control: Implications for clinical practice from the semi-structured interviews

Health professionals need to include discussions at clinic appointments about effective strategies to cope with situations that are challenging for women with GDM when family, friends and work colleagues offer unhealthy food and do not understand the importance of regular CBG monitoring (Table 6.1). Health service provision may need to consider including on-going assessment of a woman's mental well-being and an increased awareness among health professionals that some women with GDM do not share their diagnosis of GDM (Table 6.1). Direct phone access to multi-disciplinary health professionals, provision of free CBG monitoring equipment, free health shuttles, free child care when attending clinic appointments and reduce clinic waiting times all may be considered for clinical practice implications (Table 6.1).

3. Support for optimal glycaemic control: Considerations for future research from the semi-structured interviews

There appears to be an urgent need for further research in the area of support for women with GDM, as there is limited research available in the literature about the effectiveness of regular mental health

assessment for women with GDM, about the effect of a GDM diagnosis on partners and family members and effective copying strategies and about how partners and families can best support a woman with GDM in their context (Table 6.1). There are no face-to-face support or social media groups available in New Zealand. Further research could explore and/or compare if these support groups make a difference for women with GDM for maintaining optimal glycaemic control (Table 6.1).

It is of interest to note that the survey and the semi-structured interview identified similar but also some different barriers and enablers for women with GDM. Further research could explore these differences and similarities and assess if one method of identifying barriers and enablers is more effective than the other or if a mixed-method design is more comprehensive to identifying barriers and enablers to achieve optimal glycaemic control for women with GDM (Table 6.1).

6.5 Overall conclusions from this thesis

This thesis presented a comprehensive Cochrane Overview of the current evidence on treatments for women with GDM. The Overview provided a summary of the effects on relevant health outcomes of different treatments for women with GDM and identified remaining research gaps. A lack of quality evidence was found in the prepared Cochrane systematic review on the optimal glycaemic treatment targets for women with GDM and identified the need for large multi-centred well-conducted randomised trials. The thesis presents many multidimensional barriers and enablers identified by women with GDM aiming to achieve optimal glycaemic control. Health professionals with the Diabetes in Pregnancy Services will need to consider these for strategic planning and how best to provide care for women with GDM in New Zealand to achieve optimal glycaemic control.

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