Dietary and Lifestyle Advice for Women to Prevent and Treat Pregnancy Hyperglycaemia: Identifying and Closing Research Gaps

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INDEX

Pages

Table of contents

Pages

List of tables and figures

pages

List of abbreviations

ABS	Australian Bureau of Statistics
ACHOIS Trial	Australian carbohydrate intolerance study in pregnant women trial
ADA	America Diabetes Association
ADIPS	Australasian Diabetes in Pregnancy Society
ACOG	American College of Obstetricians and Gynaecologists
AIHW	Australian Institute of Health and Welfare
BGL	blood glucose level
bGDM	borderline gestational diabetes mellitus
BMI	body mass index
BP	blood pressure
CDA	Canadian Diabetes Association
CI	confidence intervals
COREQ	consolidated criteria for reporting qualitative research
cyclic GMP	cyclic guanosine monophosphate
CYWHS	the Children, Youth and Women's Health Service
dl	decilitres
DM	diabetes mellitus
EASD	European Association for the Study of Diabetes
g	grams
GDM	gestational diabetes mellitus
GI	glycaemic index
h	hour
HAPO Study	hyperglycaemia and adverse pregnancy outcome study

HBGM	home blood glucose monitoring
HDL	high-density lipoprotein
HR	heart rate
HRmax	max heart rate
IADPSG	International Association of Diabetes and Pregnancy Study Groups
IDEAL Study	investigation of dietary advice and lifestyle for women with borderline gestational diabetes
IDF	international diabetes federation
IGTP	impaired glucose tolerance of pregnancy
IOM	Institute of Medicine
IUGR	intrauterine growth restriction
kg	kilos
L	litres
LGA	large-for-gestational age
m	meters
mg	milligrams
MiG Trial	metformin in gestational diabetes trial
mm Hg	millimetres of mercury
mmol	millimoles
MODY	maturity-onset diabetes of the young
MOH	Ministry of Health
NA	not applicable
NDDG	National Diabetes Data Group
NICE	National Institute for Health and Clinical Excellence

NIH	National Institutes of Health
NIPerIER	National Institute of Perinatology Isidro Espinosa de los Reyes
NZ	New Zealand
OGCT	oral glucose challenge test
OGTT	oral glucose tolerance test
RANZCOG	Royal Australian and New Zealand College of Obstetrics and Gynaecology
RR	relative risk
RCT	randomised controlled trial
SD	standard deviation
SEIFA	socio-economic indexes for areas
SGA	small-for-gestational age
SMBG	self-monitored blood glucose
T1DM	type1 diabetes mellitus
T2DM	type 2 diabetes mellitus
WCH	Women's and Children's Hospital
WHO	World Health Organization
WOMBAT	Women and babies health and wellbeing: action through trials
wk	weeks
yr	years

Abstract

Background

Increased glycaemia during pregnancy is associated with adverse health outcomes for women and their babies. This thesis aimed to investigate and evaluate the strategies used for preventing, diagnosing and managing pregnancy hyperglycaemia.

Methods

Research methodologies used included Cochrane systematic review, qualitative semi-structured interview and a follow-up cohort study of women and babies within a randomised trial.

Results

Three Cochrane systematic reviews were conducted in identified research gaps. The first review assessed the effects of physical exercise for preventing gestational diabetes mellitus (GDM). Evidence from five randomised controlled trials involving 922 women and their babies suggested no differences in the incidence of GDM, caesarean section or operative vaginal birth between women who received additional exercise interventions and those having routine antenatal care.

The second review assessed nine randomised trials involving 429 women and 436 babies investigated eleven different types of dietary advice within six different comparisons. No one type of dietary advice was more effective than others in reducing the risk of caesarean section, operative vaginal birth, large-for-gestational age or macrosomic infants.

The third review assessed the effects of different types of management strategies for pregnant women with borderline GDM. Evidence from four randomised controlled trials involving 521 women and their babies suggested additional interventions, including dietary counselling and metabolic monitoring, helped reduce the number of macrosomic and large-for-gestational-age babies without increasing the risks of caesarean section or operative vaginal birth. All three systematic reviews highlighted the need for further, larger, well-designed trials.

The qualitative semi-structured interview study explored women's views on their diagnosis and management for borderline GDM. Twenty-two women attended the interviews. The diagnosis of borderline GDM caused concern for one third of women. The majority of women believed managing their borderline GDM was important and they planned to improve their lifestyle. Factors affecting women's ability to achieve intended lifestyle changes varied greatly. The most important enabler was thinking about baby's health. The most significant barrier was a lack of family support.

The follow-up cohort study within a randomised trial followed 245 mother-baby pairs at four to 12 months after birth to assess their health. Additional lifestyle interventions during pregnancy for women with borderline GDM had no impact on primary outcomes of maternal weight retention at four months postpartum or their babies' weight at four to 12 months of age, or any secondary outcomes, except infant subcutaneous adiposity at four months of age.

Conclusion

Synthesis of available evidence on different strategies for preventing and managing pregnancy hyperglycaemia does not yet permit clear guidance for clinical practice but indicates the need for further trials with long-term follow up to assess impact on

mothers and their children. A diagnosis of borderline GDM appears to be a powerful motivator for women to change diet and exercise patterns. As new health knowledge becomes available from further completed trials, a timely update of the relevant Cochrane reviews to include these trials is warranted.

Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future be used in a submission for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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1 Literature review on prevention and management of hyperglycaemia in pregnant women

1.1 Introduction

Maternal hyperglycaemia is a major complication of pregnancy and strong predictor for future type 2 diabetes mellitus (T2DM) (IADPSG 2010). Any degree of glucose intolerance with onset or first recognition during pregnancy is defined as gestational diabetes mellitus (GDM) (Metzger and Coustan 1998). GDM usually resolves following birth, but women who experience GDM are at increased risk of developing T2DM in the future (Bellamy et al 2009; Kim et al 2002) and their offspring are at risk of childhood obesity and the metabolic syndrome (Harder et al 2009; Mulla et al 2010; Rizzo et al 1997; Whincup et al 2008; Yogev and Visser 2009; Young et al 2002).

The diagnosis of GDM remains controversial due to the lack of universal acceptance of a particular set of diagnostic criteria (Yogev et al 2009). In fact, lack of consensus on GDM diagnostic criteria stems from a lack of consensus as to what degree of hyperglycaemia is worth diagnosing and treating (Sacks 2009). The HAPO (Hyperglycaemia and Adverse Pregnancy Outcome) Study showed morbidity associated with hyperglycaemia could occur at quite low degrees of maternal hyperglycaemia, with increasing maternal glucose concentrations showing a continuous relationship with adverse pregnancy outcomes (Metzger et al 2008).

The prevalence of GDM is increasing worldwide in parallel with the higher rates of maternal obesity and T2DM (Mulla et al 2010). Identifying effective strategies to prevent GDM are needed. Current management for GDM includes providing diet and

lifestyle advice, use of oral glucose-lowering agents, administration of insulin, maternal glucose monitoring and fetal surveillance (Alwan et al 2009).

Intensive treatment for GDM has been shown to improve pregnancy outcomes (Alwan et al 2009). It remains unclear whether such treatment for pregnant women who have milder hyperglycaemia where specific conventional diagnostic criteria for GDM are not met, is beneficial in the short and long term.

1.2 Hyperglycaemia and gestational diabetes mellitus

Hyperglycaemia is a condition in which an excessive amount of glucose circulating in the blood plasma, adversely influences health of mother and baby (Metzger and Coustan 1998). Hyperglycaemia can be triggered by drugs, such as beta blockers, epinephrine and corticosteroids; critical illness, such as stroke or myocardial infarction; physiological stress, like infection and inflammation (Capes et al 2001; Cetin et al 1994).

Persisting chronic hyperglycaemia most commonly occurs in diabetes mellitus, and is the defining characteristic of the disease (Sermer et al 1998). Hyperglycaemic disorders during pregnancy or GDM are most commonly tested for and diagnosed at 24 to 28 weeks of gestation (Ryan 2003). A diagnosis of GDM does not exclude the possibility of unrecognized T2DM before pregnancy, leading to recent calls for assessment of glucose intolerance early in pregnancy in women at risk (IADPSG 2010). In fact, GDM is often considered to be T2DM unmasked by pregnancy (Bottalico 2007). It is estimated that unrecognised T2DM accounts for about 6% of GDM diagnoses (Russell et al 2008).

1.3 Aetiology and pathogenesis of hyperglycaemia in pregnancy

Insulin, secreted by pancreatic beta cells in response to increasing maternal blood glucose concentrations in pregnancy, helps to achieve normal blood glucose concentrations. Either inadequate insulin secretion, such as in Type 1 diabetes mellitus (T1DM) or insulin resistance (defined as insulin acting less effectively in promoting glucose uptake), such as in Type 2 diabetes mellitus (T2DM) or GDM, can result in hyperglycaemia (Petry 2010).

Insulin resistance increases as pregnancy progresses (Ragnarsdottir and Conroy 2010). It is believed that the increasing insulin resistance, especially during the third trimester of pregnancy, helps to meet the increased nutrient requirement for fetal development and promotes fetal growth (Devlieger et al 2008; Ragnarsdottir and Conroy 2010). Diabetogenic hormones secreted from the placenta, including tumour necrosis factor-alpha (TNF-α), placental lactogen, placental growth hormone, cortisol and progesterone, are thought to be the likely triggers of this physiological change (Clapp 2006; Devlieger et al 2008; Ragnarsdottir and Conroy 2010; Ryan 2003).

In normal pregnancy, physiological insulin resistance can be compensated for by increased maternal insulin section. Therefore, normal maternal glycaemia is maintained (LeRoith 2002; Ryan 2003). In contrast, when insulin secretion is inadequate for the degree of insulin resistance, a hyperglycaemic disorder or GDM occurs (Clapp 2006) (LeRoith 2002).

For a woman with a pregnancy complicated by a hyperglycaemic disorder, there can be multiple contributing factors. For instance, inadequate insulin secretion and impaired insulin action frequently coexist in the same woman; therefore, it is hard to decide

which factors are the primary cause of the hyperglycaemia in a particular women (ADA 2009).

Three possible mechanisms for pregnancy hyperglycaemia are higher insulin resistance when compared with normal glucose tolerance in pregnancy, pancreatic β-cell dysfunction and genetic predisposition (Devlieger et al 2008; LeRoith 2002; Metzger et al 2007; Ragnarsdottir and Conroy 2010).

1.3.1 Higher insulin resistance when compared with a normal glucose tolerance in pregnancy

Higher than usual insulin resistance may be caused by the combination of physiological insulin resistance during pregnancy and acquired or chronic insulin resistance (Ragnarsdottir and Conroy 2010). Chronic insulin resistance is usually present before pregnancy and is exacerbated by the physiological changes during pregnancy (Metzger et al 2007; Morisset et al 2010).

1.3.2 Pancreatic β-cell dysfunction

Some pregnant women with hyperglycaemic disorders or GDM have lower insulin secretion for their degree of insulin resistance when compared with women with normal glucose tolerance (Ragnarsdottir and Conroy 2010). The possible causes are deteriorating β-cell function in relation to chronic insulin resistance or autoimmune β-cell dysfunction (LeRoith 2002; Morisset et al 2010).

1.3.3 Genetic predisposition

A small group of women (less than 6%), diagnosed with GDM have pre-existing, undiagnosed monogenic forms of diabetes such as maturity-onset diabetes of the young (MODY) and mitochondrial diabetes (Alberti et al 2004; Metzger et al 2007). These

conditions normally have early onset but relatively mild hyperglycemia, hence they may only be detected by routine antenatal glucose screening and diagnosed as GDM (Alberti et al 2004). This group of women often do not have evidence of chronic insulin resistance although the genes involved in the conditions appear to have important effects on β-cell function (Bloomgarden 2004).

1.4 Risk factors for Gestational Diabetes Mellitus

There are a wide range of known factors which can increase the risk of developing hyperglycaemic disorders during pregnancy or GDM. These are described in more detail below and include advanced age at conception, pre-pregnancy overweight or obesity, excessive weight gain since age of 18 years, excessive weight gain during pregnancy, history of having a macrosomic infant, previous history of GDM, family history of diabetes mellitus, high or low maternal birth weight, ethnicity, parity, polycystic ovarian syndrome, diet with low fibre and high glycaemic load and physical inactivity.

1.4.1 **Advanced age at conception**

Due to age-related decreased pancreatic β-cell reserve, the risk of developing GDM rises with increasing maternal age (Solomon et al 1997). An annual increased risk of 4% was reported for women aged from as young as 25 years (Solomon et al 1997). Women aged 40 years or older are twice as likely to develop GDM when compared with women aged at 25 to 29 years (Solomon et al 1997). In Australia, data from the Australian Institute of Health and Welfare (AIHW) showed that the risk of GDM increased from 1% among 15 to 19 year old women to 13% among women aged 44 to 49 years in 2005–2006 (AIHW 2008). In 2007–08, about 5.0% of females aged 15 to 49 years who gave

birth in hospital were diagnosed with GDM, with more than one-third of cases occurring among females aged 35 years and over (AIHW 2010).

1.4.2 **Pre-pregnancy overweight or obesity**

Being overweight (Body Mass Index (BMI) 25-30 kg/m^2) or obese (BMI $\geq$ 30kg/m^2) pre-pregnancy is a strong predictor for developing hyperglycaemia during pregnancy (Morisset et al 2010; Torloni et al 2009). Insulin resistance is common in overweight or obese women (Barbour et al 2007; Metzger et al 2007). Transmission of the insulin signal to enable glucose uptake results from the phosphorylation of the insulin receptor tyrosine (Ryan 2003). Significantly decreased maximal insulin receptor tyrosine phyosphorylation in muscle in overweight or obese women is a possible mechanism for additional insulin resistance in this group of women (Barbour et al 2007; Metzger et al 2007).

1.4.3 **Excessive weight gain since age of 18 years**

Excessive weight gain since the age of 18 years is associated with increased risk of GDM (Solomon et al 1997; Yeung et al 2010). Based on the Nurses' Health Study II, women who gain 20 kg or more from 18 years of age to year 1989 had 3.5-fold increased risk of developing GDM (Solomon et al 1997). This relationship is independent of maternal age, BMI at age 18 years, family history of diabetes in a first-degree relative, parity, ethnicity and prepregnancy physical activity level (Solomon et al 1997). More recently, data from 21,647 women in the Nurses' Health Study II suggests maternal weight gain since adolescence is significantly and positively associated with GDM (Yeung et al 2010).

1.4.4 **Excessive gestational weight gain during pregnancy**

Excessive weight gain during pregnancy, especially in early pregnancy, is a risk factor for pregnancy hyperglycaemia (Carreno et al 2012; Gibson et al 2012; Hedderson et al 2010; Tovar et al 2009). Evidence from non-randomised studies have consistently shown that higher gestational weight gain during early pregnancy (before 24 weeks gestation) significantly increased the risk of developing GDM (Gibson et al 2012; Hedderson et al 2010). The relationship is stronger among women who are overweight or obese before pregnancy (Gibson et al 2012; Hedderson et al 2010; Kieffer et al 2001; Saldana et al 2006). Obese women who have excessive gestational weight gain have a three to four fold increase in the risk of having pregnancy hyperglycaemia (Tovar et al 2009).

1.4.5 **History of having a macrosomic infant**

Having a macrosomic infant in a previous pregnancy is reported as a strong risk factor for GDM (Cypryk et al 2008). Women with a history of giving birth to a macrosomic baby are five times more likely to develop GDM in a subsequent pregnancy when compared with women who have given birth to normal birthweight children (Cypryk et al 2008).

1.4.6 **Previous history of GDM**

A history of GDM is a predictor of developing GDM again (Kim et al 2007). The reported recurrence rate of GDM varies between 30% and 84% (Kim et al 2007) and the rate is influenced by parity, BMI, early diagnosis of GDM, insulin requirement, weight gain, the interval between pregnancies and ethnicity (Ben-Haroush et al 2004; Kim et al 2007).

1.4.7 **Family history of Diabetes Mellitus**

A family history of diabetes mellitus, especially in a first-degree relative increases the risk of GDM (Cypryk et al 2008; Solomon et al 1997). The risk for GDM was greatest when both parents have a history of diabetes mellitus (Solomon et al 1997).

1.4.8 **High or low maternal birthweight**

Evidence from cohort studies has suggested low or high maternal birthweight is associated with increased risk of GDM (Petry 2010). Innes and colleagues found the women's birth weight had a U- shaped relationship to that woman's risk of GDM in her first pregnancy (Innes et al 2002). The odds ratio adjusted for gestational age was 2.16 (95% CI 1.04-4.50) for maternal birth weight of less than 2000 g and 1.53 (95% CI 1.03-2.27) for a birth weight of ≥4000 g (Innes et al 2002).

1.4.9 **Ethnicity**

Women with African-American, Asian-American, native American, African, Hispanic, Asian and Pacific islanders and Australian Aboriginal and Torres Strait Islander ethnicity are at higher risk of GDM when compared with Caucasian women (ADA 2009; Metzger and Coustan 1998; Solomon et al 1997). These ethnicities are similar to those at high risk of type 2 diabetes mellitus. Therefore, for a given population and ethnicity, the risk of GDM reflects the underlying frequency of type 2 diabetes (Ben-Haroush et al 2004).

In Australia, Aboriginal and Torres Strait Islander women are at higher risk when compared with other Australian women (AIHW 2008). In 2005-06, the age-adjusted incidence rate of GDM among Indigenous Australian women was 1.5 times that of other Australian women (AIHW 2008). Additionally, the risk of GDM was higher among

Indigenous women compared with other Australian women across all age groups (AIHW 2008). Indigenous Australian women aged 15 to 29 years accounted for 51% of GDM cases in 2005-06, compared with 30% among other Australian ethnicities in this age group (AIHW 2008).

1.4.10 **Parity**

Higher parity is associated with increased risk of developing hyperglycaemic disorder or GDM (Cypryk et al 2008). The risk of GDM is significantly increased in women who have had three or more previous pregnancies (Cypryk et al 2008).

1.4.11 **Polycystic ovarian syndrome**

Polycystic ovarian syndrome is a medical condition associated with insulin dysfunction and obesity (Norman et al 2007). A large cohort study suggested that women with polycystic ovarian syndrome had a 2.4-fold increased risk of GDM as compared with women without polycystic ovarian syndrome, and the risk is independent of age, ethnicity, and parity (Lo et al 2006).

1.4.12 **Diet with low fibre and high glycemic load**

Data from a large, prospective cohort study, the Nurses' Health Study II, suggests that consumption of low fibre and high glycemic load diets is associated with increased risk for GDM (Zhang et al 2006). The combination of high glycemic load and low cereal fibre diet is found to be associated with double the risk of developing GDM when pregnant (Zhang et al 2006).

1.4.13 **Physical inactivity**

Physical exercise helps weight control and increases insulin sensitivity (Weissgerber et al 2006). Results from a prospective cohort study recruiting 1006 Hispanic women suggested that after controlling for age and pre-pregnancy BMI, higher levels of pre-pregnancy and mid-pregnancy household/care-giving activities as well as mid-pregnancy sports and exercise are associated with a reduced risk of GDM (Chasan-Taber et al 2008).

1.5 Identifying strategies that can prevent pregnancy hyperglycaemia

The risk factors for GDM share similarities with those for T2DM. The prevalence of some risk factors for GDM is increasing, such as advanced maternal age, maternal overweight and obesity, therefore there is increasing prevalence of GDM worldwide. It is important to note that hyperglycaemia during pregnancy has a trans-generational effect. This may contribute to the expected further increase in prevalence of T2DM, given the increasing prevalence of maternal overweight and obesity (Petry 2010). ***Identifying strategies that can help prevent pregnancy hyperglycaemia or GDM are therefore of urgent public health importance.***

Of the risk factors for GDM mentioned under 1.4, some are modifiable and some are not modifiable (Table 1.1). Physical inactivity, as one of the modifiable risk factors, has attracted much attention in recent years (Melzer et al 2010). A meta-analysis of non-randomised trials suggests physical activity before pregnancy or in early pregnancy significantly reduces the risk of developing GDM (Tobias et al 2011). However, another systematic review of randomised controlled trials assessing different interventions for preventing GDM suggests exercise intervention during pregnancy does not reduce the

Table 1.1 Modifiable and not modifiable risk factors for gestational diabetes

Not Modifiable	Modifiable
Advanced maternal age	Pre-pregnancy overweight or obesity
Medical history of GDM	Excessive weight gain since adolescence
Family history of diabetes mellitus	Excessive weight gain during pregnancy
History of having a macrosomic infant	Polycystic ovarian syndrome
Non-white ethnicity	Diet with low fibre and high glycaemic load
High parity (e.g. ≥3 pregnancies)	Physical inactivity
High or low maternal birthweight	

risk of developing GDM (Oostdam et al 2011). Based on the current inconsistent research findings, it is still unclear whether physical exercise intervention for pregnant women is effective in preventing glucose intolerance during pregnancy and GDM (Thangaratinam et al 2012).

Research Question 1: Can physical exercise for pregnant women reduce the risk of developing pregnancy glucose intolerance during pregnancy or GDM?

1.6 Screening for Gestational Diabetes Mellitus

Screening for GDM aims to achieve an early diagnosis with the possibility of early treatment (Tieu et al 2014). Identification and treatment may improve health outcomes; however, it may also pose unnecessary anxiety due to the screening process itself and be associated with additional health costs due to the occurrence of false positive results (Moss et al 2007; Rumbold and Crowther 2002; Tieu et al 2014).

Worldwide controversy exists in terms of the best procedure and criteria for screening for pregnancy hyperglycaemia (ACOG 2011; Mulla et al 2010; Reece et al 2009). The debate centres around:

- the sensitivity, specificity and reproducibility of the screening procedure that is recommended and adequacy to serve the intended purpose;
- the degree or severity of glucose intolerance that should be identified and treated;
- prevalence and the cost of identifying women with GDM;
- determining which women require blood glucose screening.

(ACOG 2011; Yogev et al 2009).

Systematic review of the literature shows there is currently insufficient high quality evidence from randomised clinical trials as to whether screening for GDM improves pregnancy outcomes, and which type of screening test is best (Tieu et al 2014). Various screening procedures with varying degrees of sensitivity and specificity are therefore used in current clinical practice (Reece et al 2009). Two of the most commonly used screening procedures are universal screening and selective risk-related screening (Tieu et al 2014).

In Australia, universal screening is most likely to be offered (Rumbold and Crowther 2001) and a widespread policy has been to offer all pregnant women a 50 g oral glucose challenge test (OGCT) at 26 to 28 weeks gestation (Hoffman et al 1998). For selective risk-related screening as used in the United States, pregnant women have been assessed for the risk of developing GDM against a checklist at their first antenatal visit and only those who were assessed as at higher risk of developing GDM were offered screening by a 50 g OGCT (ADA 2009).

There is no consensus on the threshold value for the 50 g GCT screening test (van Leeuwen et al 2012). Values of 7.8 mmol/L (140 mg/dl) and 7.2 mmol/L (130 mg/dl) are both used in different countries around the world (Reece et al 2009). A threshold value of 7.8 mmol/L (140mg/dl) for 1-hour 50g GCT gives a sensitivity of 80% and a false-positive rate of 13% (Carpenter and Coustan 1982; Mulla et al 2010). The lower cut-off value of 7.2 mmol/l (130 mg/dl) increases the sensitivity to nearly 100%, however, the false-positive rate rises to approximately 23% to 25% (Carpenter and Coustan 1982; Mulla et al 2010).

With risk factor screening, different professional organisations and bodies around the world list various combinations of risk factors for GDM (ACOG 2013; ADA 2009; Hoffman et al 1998; Nankervis et al 2013; NICE 2008; WHO 1999). Risk factors used in screening include: maternal age over 30 years, being overweight or obese, poor pregnancy outcome in the past, family history of T2DM, personal or family history of GDM or glucose intolerance, polycystic ovarian syndrome, and being from an high risk ethnic group (Hispanic American, African, Native American, South or East Asian, Asian American, Pacific Islands, or Indigenous Australian ancestry, particularly those who reside in westernized countries or in an urban setting) (ACOG 2013; ADA 2009; Hoffman et al 1998; Metzger et al 2007; Nankervis et al 2013; NICE 2008).

The list of recommendations for GDM screening recommended by various health bodies are detailed in Table 1.2. With the recently released consensus guidelines from the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) (IADPSG 2010), many organisations have been updating their recommendations for screening.

Table 1.2 Selected international recommendations on screening for GDM

	Screening type	Population	Testing schedule	Test period	Threshold values for diagnostic testing
WHO (WHO 1999)	Universal screening[†]	All pregnant women	75 g OGTT with fasting and a 2-h BGL	24-28 wks of gestation [*]	Fasting: ≥ 7.0 mmol/L and/ or 2-hour: ≥ 7.8 mmol/L[**]
WHO (WHO 2013)	Universal screening[†]	All pregnant women	75 g OGTT with fasting, 1-h and 2-h BGL	24-28 wks of gestation[*]	Fasting: ≥ 5.1-6.9 mmol/L and/or 1-h: ≥ 10.0 and/or 2-h: ≥ 8.5-11.0 mmol/L[**]
ADIPS (Hoffman et al 1998)	Universal/ selective screening	All pregnant women/ women with ≥1 risk factors	50 g OGCT with 1-h BGL	26-28 wks of gestation	1-h: ≥ 7.8 mmol/L
			75 g OGCT with 1-h BGL		1-h: ≥ 8.0 mmol/L
ADIPS (Nankervis et al 2013)	Universal screening	All pregnant women	75 g OGTT with fasting, 1-h and 2-h BGL	24-28 wks of gestation[*]	Fasting: ≥ 5.1mmol/L and/or 1-h: ≥ 10.0 and/or 2-h: ≥ 8.5 mmol/L[**]
MOH NZ (MOH 2013)	Universal screening	All pregnant women	50 g OGCT with 1-h BGL	24-28 wks of gestation[*]	≥ 7.8 mmol/L
ADA (ADA 2009)	Selective screening	Pregnant women with ≥ 1 risk factors	50 g OGCT with 1-h BGL	24-28 wks of gestation[*]	1-h: ≥7.2 or ≥7.8 mmol/L
ADA (ADA 2013)	Universal screening	All pregnant women	75 g OGTT with fasting, 1-h and 2-h BGL	24-28 wks of gestation[*]	Fasting: ≥ 5.1 mmol/L and/or 1-h: ≥ 10.0 and/or 2-h: ≥ 8.5 mmol/L[**]
ACOG (ACOG 2013)	Universal screening	All pregnant women	50 g OGCT with 1-h BGL	24-28 wks of gestation[*]	1-h: ≥ 7.5 mmol/L or ≥ 7.8 mmol/L
NICE (NICE 2008)	Selective screening	Pregnant women with ≥1 risk factors	75 g OGTT with fasting and a 2-h BGL	24-28 wks of gestation[*]	Fasting: ≥ 7.0 mmol/L and/ or 2-hour: ≥ 7.8 mmol/L[**]
CDA (CDA 2013)	Universal screening	All pregnant women	50 g OGCT with 1-h BGL	24-28 wks of gestation[*]	≥ 7.8-11.0 mmol/L[‡]

[†] Types of screening (universal or risk factor based selective screening) according to local burden, resources and priorities (WHO 1999; 2013); [*]Early screening in first trimester for high-risk pregnant women; [**]this criteria used for GDM diagnosis and does not require confirmation; [‡] diagnosis of GDM if 1-h BGL ≥11.1 mmol/L on 50 g OGCT.

BGL: blood glucose level; wks: weeks; WHO: World Health Organization; ADIPS: Australian Diabetes in Pregnancy Society; MOH NZ: Ministry of Health, New Zealand; ACOG: American College of Obstetricians and Gynaecologists; NICE: National Institute for Health and Clinical Excellence; CDA: Canadian Diabetes Association.

1.6.1 **Australian recommendations on screening for GDM**

The Australian Diabetes in Pregnancy Society (ADIPS) recommendations for testing and diagnosis of GDM were initially developed in 1991 (Martin 1991). These have been reviewed in 1998 (Hoffman et al 1998), 2005 (McElduff et al 2005) and most recently 2012 (Nankervis et al 2013). For the last two decades and during the time course for the studies conducted and reported in this thesis, ADIPS has recommended screening for GDM using a 50g OGCT at 26-28 weeks gestation (Hoffman et al 1998). A venous plasma glucose concentration of $\geq$ 7.8 mmol/l one hour after a 50 g OGCT or a concentration of $\geq$ 8.0 mmol/l after a 75g glucose load was regarded as a positive screen (Hoffman et al 1998).

Universal screening was recommended by ADIPS, but where resources were limited, or in areas of low incidence of GDM, selective screening based on risk factors was proposed as an alternative (Hoffman et al 1998). Following the publication of ACHOIS study in 2005, universal screening for GDM in Australia was strongly advocated by authorities (McIntyre et al 2005). An Australian survey of obstetric practice conducted in 1999 indicated that about 87% of the obstetric population was being screening for GDM (Rumbold and Crowther 2001).

More recently in Feb 2013, in the light of the evidence from HAPO study published in 2008 and in line with recommendations from the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) (IADPSG 2010; Metzger et al 2008), ADIPS have proposed new consensus guidelines for the testing and diagnosis of GDM in Australia and New Zealand in 2012 (Nankervis et al 2013). In these new ADIPS guidelines, the 50 g OGCT is no longer recommended for GDM screening (Nankervis et al 2013). A one-step, diagnostic 75g OGTT at the first opportunity after conception for

women who are at high risk of having GDM is recommended by ADIPS (Nankervis et al 2013). Women at high risk but with a normal OGTT at early pregnancy are recommended to repeat OGTT at 24-28 weeks' gestation (Nankervis et al 2013). At the time of writing this thesis, these recently released ADIPS guidelines have not been widely adopted into Australian clinical practice. The Australian National Antenatal Care Guidelines- Module 2 are currently under preparation (Australian Health Ministers' Advisory Council 2014). In New Zealand, the new draft clinical guidelines for the Ministry of Health do not recommend adoption of the new ADIPS guidelines (MOH 2013) (Table 1.2).

1.7 Diagnosis of Gestational Diabetes Mellitus

The 'perfect' diagnostic test for pregnancy hyperglycaemia has not yet been developed (Coustan et al 2010). Such a test would give high true positive and low false positive rates, with both a sensitivity and specificity of 100% (Egger 2001).

Within current clinical practice, a variety of diagnostic tests for GDM are also used, due to different recommendations from professional colleges and bodies around the world (Coustan et al 2010) (Table 1.3). To date, the most commonly used methods for GDM diagnosis are the 75-gram 2-hour oral glucose tolerance test (OGTT) and the 100-gram 3-hour OGTT. The 75-gram 2- hour OGTT is used in many countries, including Australia and New Zealand (Hoffman et al 1998; RANZCOG 2008). The 100-gram 3-hour OGTT is mainly used in the USA (Yogev et al 2009)

The currently widely used OGTT in GDM diagnosis has the limitations of lack of reproducibility (around 78%) and is expensive and inconvenient to administer (Harlass et al 1991; Reece et al 2009).

Table 1.3 Selected international recommendations on diagnosis of GDM

	Plasma BGL (mmol/L)	Plasma BGL (mg/dl)	Positive diagnosis
WHO (WHO 1999); NICE (NICE 2008)			
Fasting glucose 2-h post-75 g load	≥ 7.0 ≥ 7.8	126 140	≥ 1 value(s) is (are) met or exceeded.
WHO (WHO 2013)			
Fasting glucose 1-h post-75 g load* 2-h post-75 g load	≥ 5.1-6.9 ≥ 10.0 ≥ 8.5-11.0	92-125 180 153-199	≥ 1 value(s) is (are) met or exceeded.
ADIPS (Hoffman et al 1998)			
Fasting glucose 2-h post-75 g load	≥ 5.5 ≥ 8.0	99 144	≥ 1 value(s) is (are) met or exceeded.
ADIPS (Nankervis et al 2013)			
Fasting glucose 1-h post-75 g load 2-h post-75 g load	≥ 5.1 ≥ 10.0 ≥ 8.5	92 180 153	≥ 1 value(s) is (are) met or exceeded.
MOH NZ (MOH 2013)			
Fasting glucose 2-h post-75 g load	≥ 5.5 ≥ 9.0	99 162	≥ 1 value(s) is (are) met or exceeded.
RANZCOG (Cutchie et al 2006)			
Fasting glucose 2-h post-75 g load	≥ 5.5 ≥ 9.0	99 162	≥ 1 value(s) is (are) met or exceeded.
ACOG (ACOG 2013)**			
Fasting glucose 1-h post-100 g load 2-h post-100 g load 3-h post-100 g load	≥ 5.8 ≥ 10.6 ≥ 9.2 ≥ 8.0	105 190 165 145	≥ 2 values must be met or exceeded.
Fasting glucose 1-h post-100 g load 2-h post-100 g load 3-h post-100 g load	≥ 5.3 ≥ 10.0 ≥ 8.6 ≥ 7.8	95 180 155 140	≥ 2 values must be met or exceeded.
ADA (ADA 2009)			
Fasting glucose 1-h post-100 g load 2-h post-100 g load 3-h post-100 g load	≥ 5.3 ≥ 10.0 ≥ 8.6 ≥ 7.8	95 180 155 140	≥ 2 values must be met or exceeded.

ADA (ADA 2013)			
Fasting glucose 1-h post-75 g load 2-h post-75 g load	≥ 5.1 ≥ 10.0 ≥ 8.5	92 180 153	≥ 1 value(s) is (are) met or exceeded.
IADPSG (IADPSG 2010)			
Fasting glucose 1-h post 75 g load 2-h post 75 g load	≥ 5.1 ≥ 10.0 ≥ 8.5	92 180 153	≥ 1 value(s) is (are) met or exceeded.
CDA (CDA 2013)			
Fasting glucose 1-h post 75 g load 2-h post 75 g load	≥ 5.3 ≥ 10.6 ≥ 9.0	95 191 162	≥ 1 value(s) is (are) met or exceeded.
EASD (Brown et al 1996)			
Fasting glucose 2-h post 75 g load	6.0 9.0	108 162	≥ 1 value(s) is (are) met or exceeded.

*There are no established criteria for the diagnosis of diabetes based on the 1-h post load value (WHO 2013); **Considerations for selection of one set of diagnostic criteria over the other could include, but are not limited to, the baseline prevalence of diabetes in specific communities and the availability of resources to appropriately manage the numbers of women diagnosed with GDM by any given protocol (ACOG 2013).

WHO: World Health Organization; NICE: National Institute for Health and Clinical Excellence; ADIPS: Australian Diabetes in Pregnancy Society; MOH NZ: Ministry of Health, New Zealand; RANZCOG: Royal Australian and New Zealand College of Obstetrics and Gynaecology; ACOG: American College of Obstetrics and Gynaecology; ADA: American Diabetes Association; IADPSG: International Association of Diabetes and Pregnancy Study Groups; CDA: Canadian Diabetes Association. EASD: European Association for the Study of Diabetes.

Besides the OGTT, other tests used for the diagnosis of GDM include glycated haemoglobin, fasting blood glucose, random blood glucose or glycouria, although systematic review suggests these tests may not be as reliable as the OGTT in diagnosing pregnancy hyperglycaemia (Farrar et al 2011).

Globally, there is an overall lack of international consistency with regard to the cut-off values used for the diagnosis of GDM from an OGTT (Table 1.3). This means varying

proportions of the pregnant population are defined or labelled as having GDM in different parts of the world. The diagnosis of GDM therefore varies depending on which diagnostic criteria are used within a population or study (IADPSG, 2010). Different health bodies recommend slightly different diagnostic criteria; and the recommendations have frequently changed over time sometimes due to the changing understanding about the effects of hyperglycaemia on pregnancy outcomes (Coustan et al 2010)

In recent times, following publication of HAPO Cohort study results in 2008, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) have recommended new diagnostic cut-off values for the 75-gram 2-hour OGTT based on perinatal outcome data (IADPSG 2010). As indicated earlier, this has led some Professional Diabetes Associations and International Groups to review their own recommendation for screening and diagnosis of GDM (Coustan et al 2010; IADPSG 2010). A summary of current diagnostic criteria recommended by selected health bodies is listed in Table 1.3 (as of February 2014).

1.7.1 Recommendations in Australia and New Zealand for the diagnosis of GDM

In Australia and New Zealand, the recently released new ADIPS guidelines recommend a 75g 2-hour OGTT for the diagnosis (Nankervis et al 2013). The diagnostic criteria recommended by ADIPS for use over the last two decades have been a fasting venous plasma glucose level of $\geq$ 5.5 mmol/L (99 mg/dl) and/or $\geq$ 8.0 mmol/L (144 mg/dl) 2 hours after a 75 g glucose load (Hoffman et al 1998; Simmons et al 2008).

The International Association of Diabetes and Pregnancy Study Groups (IADPSG) new diagnostic criteria for GDM have been recommended by ADIPS in their updated

consensus guidelines published in 2013 (Nankervis et al 2013). The new IADPSG diagnostic criteria are fasting glucose concentrations ≥ 5.1 mmol/L, or 1-hour post 75 g OGTT ≥ 10.0 mmol/L or 2-hour post 75 g OGTT ≥ 8.5 mmol/L (Nankervis et al 2013). The proposed changes to the diagnostic criteria for GDM are generating widespread debate in the literature, with concern about the two to three fold increased number of women labelled as having GDM, and its related cost to the woman and health service (Cundy 2012; Holt et al 2011; Moses et al 2011; NIH 2012; Ryan 2011; 2013).

1.8 Adopting the new IADPSG criteria and prevalence of hyperglycaemic disorders during pregnancy and GDM

The prevalence of some GDM risk factors such as obesity and advancing maternal age are increasing. Combined with more universal screening, this means that the prevalence of GDM is rising worldwide (Bottalico 2007; Debelea et al 2005). In the past 20 years, the rate of GDM has increased by between 16 to 127% within different ethnic groups (Ferrara 2007).

The prevalence of GDM varies in different populations with the precise figure being unclear due to differences in screening procedure used and diagnostic criteria applied (Ben-Haroush et al 2004; Mulla et al 2010). It is estimated that around 7% of all pregnant women around the world will develop GDM (Ragnarsdottir and Conroy 2010). In low-risk populations, the estimated GDM prevalence using older diagnostic criteria is 1.4% to 2.8%; in higher risk populations, the estimated prevalence is 3.3% to 6.1% and in some very high-risk populations, the prevalence may be higher than 10% (Mulla et al 2010). In the United States, among an ethnically diverse population in California, the GDM prevalence varied between about 5% and 8.5%, with the highest rate in Asian women, lowest rate in non-Hispanic white women, and intermediate rate in black and

Hispanic women (Ferrara 2007). In Australia in 2007, the incidence of GDM varied between 2.8% and 7.1%, with the highest in Northern Territory and lowest in Tasmania (Laws and Sullivan 2009). In the United Kingdom, the National Institute for Health and Clinical Excellence (NICE) reported the prevalence of GDM in England and Wales to be 3.5% on average (varying between different ethnic population groups) (NICE 2008).

Adoption of the new criteria for diagnosis of GDM developed by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) in 2010 is predicted to significantly increase the incidence and prevalence of GDM around the world (ADA 2011; Coustan et al 2010; Hirst et al 2012; Holt et al 2011; IADPSG 2010). Based on the IADPSG criteria, the overall incidence of GDM rose to 17.8% for the cohort of women involved in the HAPO study, which included 25,505 pregnant women at 15 centres in nine countries (IADPSG 2010; Sacks et al 2012). The two Australian sites involved in HAPO were estimated to have a GDM prevalence of 12.1% in Brisbane and 13.6% in Newcastle by the new IADPSG criteria (Sacks et al 2012).

A recent study conducted in Wollongong , an Australian city with a population of 280,000 people, found the GDM prevalence increased from 9.6% to 13% by changing from the previous ADIPS criteria to IADPSG criteria (Moses et al 2011). Similarly, a 69% increase was reported for the prevalence of GDM (from 1.9% to 3.1%) in Southampton, United Kingdom by applying the new criteria in place of the WHO criteria (Holt et al 2011). In Ho Chi Minh city, Vietnam, the prevalence of GDM was estimated to be 6.1% by using the previous ADA criteria (ADA 2009) and elevated to 20.3% by using the new IADPSG criteria (Hirst et al 2012).

1.9 Health outcomes for gestational diabetes mellitus

GDM is associated with increased risk of complications for both mothers and their babies during pregnancy and after birth.

1.9.1 **Fetal outcomes for GDM when untreated**

Maternal hyperglycaemia, through transplacental passage, exposes the fetus to higher concentrations of glucose than normal (Reece et al 2009). As maternal insulin does not cross the placenta from the mother to fetus, the fetus is prompted to increase its own insulin secretion (Reece et al 2009). Excessive insulin produced by the fetus will lead to fetal over-growth. This manifests as large for gestational age (LGA); and if the birthweight is ≥ 4000 g, macrosomia (Reece et al 2009).

Being a large for gestational age fetus or a macrosomic infant is a surrogate for many of the complications associated with pregnancy hyperglycaemia (Esakoff et al 2009). Babies who are large for gestational age or macrosomic are at increased risk of injury during birth, such as shoulder dystocia, bone fractures, nerve palsies and may lead to perinatal asphyxia (Henriksen 2008; Iffy et al 2008; Langer et al 2005), even if maternal GDM is treated during pregnancy (Esakoff et al 2009).

After birth, babies born to women with hyperglycaemic disorders are at higher risk of other neonatal complications such as respiratory distress syndrome, hypoglycaemia, hyperbilirubinaemia, cardiomyopathy, hypocalcaemia, hypomagnesaemia, polycythaemia and hyperviscosity (Reece et al 2009; Soler et al 1978).

In the longer term, children born to mothers with GDM are at increased risk of being overweight or obese, of developing T1DM and T2DM mellitus and having impaired intellectual achievement (Harder et al 2009; Mulla et al 2010; Rizzo et al 1997;

Whincup et al 2008; Yogev and Visser 2009; Young et al 2002). These health problems may repeat across generations (Mulla et al 2010; Petitt et al 1985). Infants born LGA are at increased risk of developing the metabolic syndrome in childhood, adolescence and adulthood (Barker 1994; Guerrero-Romero et al 2010; Harder et al 2009). The metabolic syndrome is a cluster of risk factors defined by the occurrence of three of the following: obesity, hypertension, hypertriglyceridaemia and low HDL cholesterol concentration (Grundy et al 2004). Childhood development of the metabolic syndrome predicts adult metabolic syndrome and T2DM at 25 to 30 years of age (Morrison et al 2008). Evidence also shows LGA and macrosomia are associated with increased risk of premenopausal breast cancer (Forman et al 2005). ***Therefore, there are life-long health risks to the fetus of a woman with GDM.***

1.9.2 **Maternal outcomes for GDM when untreated**

For women with GDM, there is an increased risk of developing pre-eclampsia and an increased use of induction of labour and caesarean section compared with women who do not develop GDM (Metzger et al 2008; von Katterfeld et al 2012). Due to the risk of having a LGA or macrosomic baby, mothers are at higher risk of cephalopelvic disproportion, uterine rupture, shoulder dystocia and perineal lacerations (Jastrow et al 2010).

In the longer term, epidemiological research shows that women who have had GDM have at least a seven-fold risk of developing T2DM in future when compared with those who have had a normoglycaemic pregnancy (Bellamy et al 2009). The progression to T2DM increases steeply within first five years after giving birth, and then appears to plateau (Kim et al 2002). An Australian population based study suggests that 50% of Australian women who have GDM will develop T2DM within 10 years of delivery (Lee et al 2007).

In addition, women with a history of GDM are at significantly increased risk of developing metabolic syndrome and cardiovascular disease after childbirth (Bo et al 2006; Carr et al 2006; Di Cianni et al 2007; Lauenborg et al 2005; Retnakaran et al 2009; Vohr and Boney 2008). A cross-sectional study of 995 women found that, women with a history of GDM were more likely than those without a GDM history to have the metabolic syndrome, 86.6% versus 73.5%, $p<0.001$; cardiovascular disease,15.5% versus 12.4%, $p=0.005$, respectively (Carr et al 2006). Metabolic syndrome in this trial was defined as having three or more of the following: hypertension (blood pressure ≥ 130/85 mmHg), abdominal obesity (waist circumference >88 cm), fasting serum HDL cholesterol < 1.3 mmol/L, fasting serum triglycerides ≥ 1.7 mmol/L, and abnormal glucose tolerance (fasting plasma glucose ≥ 6.1 mmol/L) (NIH 2001). At a median of 9.8 years postpartum, the prevalence of metabolic syndrome was 43.5% in women with previous diet-treated GDM, compared with 14.8% in the non-GDM control group (Lauenborg et al 2005). Metabolic syndrome was defined slightly different in this trial as having three or more of the following: blood pressure ≥ 130/85 mmHg or receiving antihypertensive medication, waist circumference > 88 cm, HDL cholesterol < 1.3 mmol/L (50 mg/dl) or receiving drug treatment for reduced HDL, triglycerides ≥ 1.7 mmol/L (150 mg/dl) or receiving drug treatment for elevated triglycerides, and fasting plasma glucose ≥ 5.6 mmol/L (100 mg/dl) or taking anti-hyperglycaemic medication (Grundy et al 2005).

1.10 A review of the evidence base for treatment of women with GDM: specific treatment compared with standard antenatal care

Although the health risks associated with untreated GDM are well recognized, there has been much confusion surrounding whether treating GDM improves pregnancy outcomes (Hillier et al 2008; Hoffman et al 1998). Over the last ten years, a series of high quality studies and systematic reviews have clarified the benefits of detecting and treating GDM (Alwan et al 2009; Horvath et al 2010).

Alwan and colleagues systematically reviewed evidence from eight randomised controlled trials (Alwan et al 2009). When comparing any specific intervention with routine antenatal care for women with GDM, the risk of pre-eclampsia was reduced and there were no statistically significant differences in the caesarean section rate (Alwan et al 2009). For the infants of women with GDM, results suggested specific treatment reduced the risk of macrosomia (birth weight greater than 4000g) or birthweight greater than the 90th centile (Alwan et al 2009). The authors concluded that women with GDM should be considered for specific treatment, including dietary advice and insulin, in addition to routine antenatal care to improve pregnancy outcomes. In addition, further large studies comparing different alternative treatment strategies, considering different ends of the severity spectrum of glucose intolerance were needed (Alwan et al 2009).

Another systematic review conducted by Horvath and colleagues had a wider inclusion criteria for trials, and included five randomised trials with one trial assessing the effects of treatment for women with borderline glucose intolerance(Horvath et al 2010). This systematic review found the incidence of shoulder dystocia was significantly reduced in the group of women who received specific treatment ; and the number of large for gestational age infants and macrosomia was significantly lower in the specific treatment

group compared with standard care (Horvath et al 2010). This review concluded that specific treatment for GDM, consisting of treatment to lower blood glucose concentration by diet control and/ or insulin alone or with special obstetric care, seemed to lower the risk of some perinatal or neonatal complications (Horvath et al 2010). ***However, no conclusion could be made for the effects of treatment of GDM on long-term health outcomes beyond the neonatal period for both mothers and babies due to lack of relevant data*** (Horvath et al 2010).

Although both systematic reviews showed consistency of improved health outcomes for pregnant women with glucose intolerance after being managed with diet modification with or without insulin, it is still unclear which type of diet is the most effective in managing pregnancy hyperglycaemia. Previous systematic review assessing the effects of low glycaemic index (GI) diet on pregnancy outcomes suggested low GI diet reduced the needs for insulin in women with GDM when compared with those had a high GI diet (Louie et al 2010). To assess the effectiveness of different types of dietary advice in managing pregnancy hyperglycaemia, a systematic review of evidence from randomised trials is needed.

Research Question 2: What are the effects of different types of dietary advice for women with GDM on pregnancy outcomes?

1.10.1 Current recommendations on treatment and management for GDM

Ideally, treatment recommendations should be based on level 1 evidence, which is obtained from a systematic review of all relevant randomised controlled trials (Hillier et al 2011). Any recommendations on treating GDM should be based on the best available

evidence, with considerations to the quality, relevance and strength of the evidence (Hillier et al 2011).

Widely recommended interventions for GDM include: lifestyle intervention (medical nutrition therapy and physical activity), hypoglycaemic therapy (insulin or oral glucose-lowering agents), glucose concentration monitoring and fetal surveillance (IDF clinical guidelines task force 2009; Metzger et al 2007; NICE 2008). Different professional organisations and health bodies around the world have similar recommendations on management strategies for GDM (Hoffman et al 1998; IDF clinical guidelines task force 2009; Metzger et al 2007; NICE 2008; Simmons et al 2008).

1.10.2 **Management and treatment recommendations in Australia for GDM**

In Australia, the ADIPS 1998 recommendations advised a team approach in managing pregnant women with GDM (Hoffman et al 1998). If resources were available, the team would comprise an obstetrician, diabetes physician, a diabetes educator (diabetes midwifery educator), dietitian, midwife and paediatrician (Hoffman et al 1998). Antenatal fetal monitoring and fetal monitoring during labour was recommended as a part of recommended care for women with GDM (Hoffman et al 1998). Perinatal glycaemic control should be achieved by patient diet and lifestyle education, and insulin if indicated. Oral hypoglycaemic agents were not recommended for use by ADIPS originally (Hoffman et al 1998); although with the publication of the Metformin in Gestational Diabetes Trial (the MiG Trial) (Rowan et al 2008), metformin therapy is increasingly being used in many centres around Australia and New Zealand and globally (Donovan and McIntyre 2010; Goh et al 2011).

Based on observational data, the only data available, ADIPS recently proposed new consensus guidelines (Nankervis et al 2013). In the new consensus guidelines, glucose

targets values for self-monitoring blood glucose have been reduced to fasting ≤ 5.0mmol/L, 1-h after a meal ≤ 7.4 mmol/L, and 2-h blood after a meal ≤ 6.7 mmol/L (Nankervis et al 2013). The new ADIPS guidelines do not mention management strategies for GMD (Nankervis et al 2013).

1.11 Evidence for management and treatment of Borderline Gestational Diabetes Mellitus

1.11.1 Introduction

For some women whose glucose concentrations do not meet diagnostic criteria for GDM, their glucose concentration may still be too high to be considered as normal. These women can be at increased risk of adverse pregnancy outcomes and treatments lowering blood glucose concentrations may be beneficial for them (Bonomo et al 2005; Ju et al 2008). Women with blood glucose concentrations in this intermediate range are referred to as having borderline GDM.

Risk factors for developing borderline GDM are similar to those for GDM previously discussed in section 1.4. The prevalence of borderline GDM is reported as being between 7% and 8.8% (Dodd et al 2007; Rumbold et al 2006; Stamilio et al 2004).

1.11.2 Perinatal health outcomes of untreated pregnant women with intermediate glucose intolerance without meeting current diagnostic criteria for GDM – evidence from observational studies

Observational studies have been conducted in different countries to investigate the effects of mild hyperglycaemic disorders during pregnancy (which do not meet the criteria for a GDM diagnosis) on maternal and infant health outcomes (Carr et al 2006;

Hedderson et al 2003; Ju et al 2008; Metzger et al 2008; Retnakaran et al 2009; Sermer et al 1998; Stamilio et al 2004; Vambergue et al 2008; Yogev et al 2004).

In the US, Yogev and colleagues recruited 1813 women and reported an association between increasing hyperglycaemia and the risk of pre-eclampsia (Yogev et al 2004). Hedderson and colleagues found the risk of spontaneous preterm birth increased with increasing levels of pregnancy glycaemia (Hedderson et al 2003). In Stamilio's study, a false-positive glucose challenge test was found to be associated with significantly increased risks of maternal composite adverse outcomes (including preeclampsia, chorioamnionitis, and postpartum endometritis), endometritis, shoulder dystocia, macrosomia (birthweight > 4500g) (Stamilio et al 2004). The false-positive glucose challenge test was defined in this study as a positive 1-hour 50-gram OGCT ($\geq$ 7.5 mmol/l (135 mg/dl)) followed by a negative 100-gram 3-hour OGTT (fasting < 5.6 mmol/l (100 mg/dl), 1-hour < 10.6 mmol/l (190 mg/dl), 2-hours < 9.2mmol/l (165 mg/dl), 3-hours < 8.1 mmol/l (145 mg/dl)) (Stamilio et al 2004).

The Toronto Tri-Hospital study found increasing degrees of carbohydrate intolerance to be associated with an increased risk of pre-eclampsia, caesarean section, macrosomia, and need for neonatal phototherapy (Sermer et al 1998).

In Australia, Ju and colleagues reported maternal obesity and increasing maternal age were associated with increased risk of developing borderline GDM (defined as women with a positive OGCT (plasma blood glucose $\geq$ 7.8mmol/L 1 hour after a 50 g glucose load) and a normal 75 g OGTT (fasting blood glucose < 5.5 mmol/L and 2 hour blood glucose < 7.8mmol/L)) (Ju et al 2008). Borderline GDM was a strong indicator of adverse maternal health outcome (defined as any of the following until six weeks postpartum: death, pulmonary oedema, eclampsia, stroke, thrombocytopaenia, renal insufficiency, respiratory arrest, placental abruption, abnormal liver function, pre-term

prelabour rupture of membranes, major postpartum haemorrhage, postpartum, pyrexia, pneumonia, deep-vein thrombosis, or pulmonary embolus requiring anticoagulant therapy) (Ju et al 2008).

Women with borderline GDM were more likely to have a higher rate of adverse maternal health outcomes, pregnancy induced hypertension, a caesarean for fetal distress, and require a longer postnatal hospital stay than those with normal glucose tolerance (Ju et al 2008) (Table 1.4).

Table 1.4 Clinical outcomes among women with borderline GDM (140 women) compared with women with a normal OGCT (1596 women)

	Unadjusted RR [95% CI]	**P value**	**Adjusted RR [†] [95% CI]**	**P value**
Maternal adverse outcome[‡]	**1.59 [1.00, 2.52]**	**0.05**	1.47 [0.92, 2.34]	0.11
Pregnancy induced hypertension	**1.51 [1.03, 2.20]**	**0.03**	1.31 [0.90, 1.90]	0.16
Caesarean section for fetal distress	**1.63 [1.10, 2.41]**	**0.01**	1.43 [0.97, 2.11]	0.07
Maternal length of stay (days)[§]	**0.4 [0.1, 0.7]**	**0.01**	0.3 [-0.0, 0.6]	0.06

[†]Adjusted for maternal age and body mass index; [‡]maternal adverse outcomes defined as any of the following until six weeks postpartum: death, pulmonary oedema, eclampsia, stroke, thrombocytopenia, renal insufficiency, respiratory arrest, placental abruption, abnormal liver function, pre-term prelabour rupture of membranes, major postpartum haemorrhage, postpartum, pyrexia, pneumonia, deep-vein thrombosis, or pulmonary embolus requiring anticoagulant therapy. [§]Effects are mean difference (95% CI).
RR: relative risk; CI: confidence interval.

Source: (Ju et al 2008)

Babies born to women with borderline GDM were more likely to be preterm, macrosomic (birthweight ≥ 4500g), admitted to the neonatal intensive care unit or the neonatal nursery and have a longer hospital stay when compared with those born to women with normal glucose tolerance (Ju et al 2008) (Table 1.5). After adjusting for maternal age and BMI, only the difference in the risk of admission to a nursery or neonatal intensive care unit remained significant between the two groups (Ju et al 2008) (Table 1.4 and Table 1.5).

Table 1.5 Clinical outcomes among babies born to women with borderline GDM (139 babies) compared with women with a normal OGCT (1583 babies)

	Unadjusted RR [95%CI]	**P value**	**Adjusted RR [95%CI]***	**P value**
Preterm birth (<37 weeks)	**1.68 [1.00, 2.80]**	**0.05**	1.64 [0.97, 2.75]	0.06
Macrosomia (birthweight ≥4.5 kg)	**2.53 [1.06, 6.03]**	**0.04**	2.27 [0.97, 5.34]	0.06
Admission to nursery	**1.42 [1.14, 1.76]**	**0.002**	**1.35 [1.09, 1.68]**	**0.01**
Admission to NICU	**2.18 [1.09, 4.36]**	**0.03**	**2.05 [1.02, 4.13]**	**0.04**

*adjusted for maternal age and body mass index. NICU: neonatal intensive care unit; RR: relative risk; CI: confidence interval.

Source: (Ju et al 2008)

Table 1.6 Adjusted odds ratios for associations between maternal glycaemia as a continuous variable and primary and secondary perinatal outcomes in the HAPO Study†

	Plasma glucose level		
	Fasting	At 1 hour	At 2 hours
	Odds ratio (95% CI)		
Primary outcomes			
Birth weight > 90th centile	**1.38 (1.32, 1.44)**	**1.46 (1.39, 1.53)**	**1.38 (1.32, 1.44)**
Primary caesarean section‡	**1.11 (1.06, 1.15)**	**1.10 (1.06, 1.15)**	**1.08 (1.03, 1.12)**
Clinical neonatal hypoglycaemia	1.08 (0.98, 1.19)*	**1.13 (1.03, 1.26)**	**1.10 (1.00, 1.12)**
Cord-blood C-peptide > 90th percentile	**1.55 (1.47, 1.64)**	**1.46 (1.38, 1.54)**	**1.37 (1.30, 1.44)**
Secondary outcomes			
Preterm birth (before 37 week)	1.05 (0.99, 1.11)	**1.18 (1.12, 1.25)**	**1.16 (1.10, 1.23)**
Shoulder dystocia or birth injury	**1.18 (1.04, 1.33)**	**1.23 (1.09, 1.38)**	**1.22 (1.09, 1.37)**
Intensive neonatal care	0.99 (0.94, 1.05)	**1.07 (1.02, 1.13)**	**1.09 (1.03, 1.14)**
Hyperbilirubinaemia	1.00 (0.95, 1.05)	**1.11 (1.05, 1.17)**	**1.08 (1.02, 1.13)**
Preeclampsia	**1.21 (1.13, 1.29)**	**1.28 (1.20, 1.37)**	**1.28 (1.20, 1.37)**

†Odds ratios of outcomes for an increase in the glucose concentration of 1 standard deviation (0.4 mmol/L [6.9 mg/dl] for the fasting plasma glucose level, 1.7 mmol/L [30.9 mg/dl] for the 1-hr plasma glucose concentration, and 1.3 mmol/L [23.5 mg/dl] for 2-hr plasma glucose concentration). The model for preeclampsia did not include adjustment for hospitalisation or mean arterial pressure, and presence or absence of family history of hypertension or antenatal urinary tract infection was included in the model for preeclampsia only. ‡Data for women who had had a previous caesarean section were excluded. *The P value for the quadratic (nonlinear) association was 0.013.

Source: (Metzger et al 2008)

The HAPO study (recruiting 25,505 women from 9 countries and 15 centres) confirmed the association of higher perinatal risks with increasing maternal hyperglycaemia (Metzger et al 2008). This large multi-centre and multi-ethnic cohort study found the adverse effects of maternal hyperglycaemia on the pregnancy outcomes did not occur at specific thresholds but increased on a continuum with increasing hyperglycaemia (Metzger et al 2008). Adjusted odds ratios for associations between maternal glycaemia as a continuous variable and perinatal outcomes are detailed in Table 1.6.

1.11.3 A review of the evidence base for treatment of women with glucose intolerance not meeting current diagnostic criteria for GDM

Although intensive management of GDM has proven beneficial for women with GDM and their babies (Alwan et al 2009; Horvath et al 2010), much less is known about the effects of managing pregnancy hyperglycaemia not meeting diagnostic criteria on the immediate health outcomes for women and their babies or on their later health.

Research Question 3: What are the effects of different types of management strategies for pregnant women with hyperglycaemia not meeting diagnostic criteria for GDM?

1.11.4 Diagnosis of glucose intolerance not meeting current diagnostic criteria for GDM - impact on the women of diagnosis - evidence from qualitative studies

Based on the results from HAPO study, the relationship between increased hyperglycaemia and the adverse pregnancy outcomes appears to be continuous (Metzger

et al 2008). There are no immediately obvious cut-off points which can be labelled as abnormal to diagnose GDM (Metzger et al 2008). It is therefore unclear what degree of pregnancy hyperglycaemia is worth diagnosing and treating.

A diagnosis of pregnancy hyperglycaemia may cause significant psychological impact on women and their families. For women with GDM, a few qualitative studies have been conducted in different populations to investigate the psychological impacts of screening and/or the diagnosis of GDM during pregnancy (Bandyopadhyay et al 2011; Hirst et al 2012; Hjelm et al 2005; Hjelm et al 2008; Kerbel et al 1997; Rumbold and Crowther 2002).

Negative feelings about a diagnosis of GDM, including "worried", "scared" or "shocked", have been expressed by women in different studies (Bandyopadhyay et al 2011; Hirst et al 2012; Hjelm et al 2005; Hjelm et al 2008; Kerbel et al 1997). A survey based qualitative study suggested women with a screening positive test for GDM had lower health perceptions, were less likely to rate their health as "much better than one year ago" and were more likely to only rate their health as "fair" rather than "very good" or "excellent" when compared with women screening negative (Rumbold and Crowther 2002).

Women's experience about lifestyle self-management for GDM has also been investigated in previous studies (Carolan et al 2012; Evans and O'Brien 2005; Hirst et al 2012). Enablers and inhibitors have been considered important to women's ability to achieve lifestyle self-management and therefore have been explored by researchers involving women from different ethnic groups (Carolan et al 2012; Evans and O'Brien 2005; Hirst et al 2012).

There is very limited evidence on women's views towards a diagnosis of less severe pregnancy hyperglycaemia and their attitudes towards management of this intermediate form of pregnancy hyperglycaemia.

Research Question 4: What are women's experiences after being diagnosed with pregnancy hyperglycaemia not meeting current GDM diagnostic criteria?

1.11.5 Longer health outcomes of pregnant women with glucose intolerance not meeting current diagnostic criteria for GDM – evidence from observational studies

Some evidence from a few previous observational studies have suggested even mild forms of pregnancy hyperglycaemia are associated with long term adverse health outcomes for both women and their children (Bo et al 2006; Retnakaran et al 2010; Retnakaran et al 2009; Stuebe et al 2011). Observational studies have suggested that the risk of developing metabolic syndrome increase progressively from women who were normoglycaemic to those with GDM (Retnakaran et al 2010; Retnakaran et al 2009). By three month postpartum, the prevalence of metabolic syndrome was increased from 10% in women with normal glucose tolerance to 17.6% in women with gestational impaired glucose tolerance, and to 20.0% in women with GDM (Retnakaran et al 2010). Bo and colleagues reported similar findings where the prevalence of metabolic syndrome was six-fold higher in women with previous GDM and two-fold higher in women with previous positive OGCT and negative OGTT, than in women with previous normal glucose tolerance (Bo et al 2006). The difference was independent of confounding factors of maternal age, maternal BMI, diabetes history in first-degree relatives, smoking, education level and exercise (Bo et al 2006). Similar findings were reported by another community-based prospective cohort study (Stuebe et al 2011).

Stuebe and colleagues reported gestational impaired glucose tolerance and GDM were associated with an adverse metabolic profile at three years postpartum, and were independent of BMI and parental history of diabetes (Stuebe et al 2011).

For longer term health outcomes for children born to women with mild pregnancy hyperglycaemia without meeting the diagnostic criteria for GDM, an US cohort study involving 9,439 multi-ethnicity mother-child pairs found that the risk of obesity in offspring at 5 to 7 years of age was increased and linked to increasing maternal hyperglycaemia (Hillier et al 2007). In addition, offspring of women with pregnancy hyperglycaemia were more likely to develop glucose intolerance or T2DM and metabolic syndrome during childhood and young adulthood (Clausen et al 2008; Franks et al 2006; Iqbal et al 2009; Malcolm et al 2006; Silverman et al 1995; Wroblewska-Seniuk et al 2009). Compared with offspring of women with normoglycaemia pregnancies, the odds ratios for type 2 diabetes or impaired glucose tolerance or impaired fasting glucose were 7.76 in offspring of diet-treated GDM mothers and 4.46 in offspring of women with elevated fasting blood glucose, but a normal OGTT (Clausen et al 2008). By the age of 22 years, the prevalence of type 2 diabetes or pre-diabetes were 21% for offspring born to mothers with diet-treated GDM; 12% for those born to women with an elevated fasting blood glucose, but a normal OGTT; and only 4% for offspring born to women with normal glycaemia during their pregnancies (Clausen et al 2008).

Research Question 5: What are the effects of additional care including dietary and lifestyle advice compared with standard care for pregnant women with hyperglycaemia not meeting current diagnostic criteria for GDM on the health outcomes for women and their babies at 4 months after the birth?

1.12 Summary of research gaps identified

Adverse pregnancy outcomes have been consistently reported in women with increased glycaemia during pregnancy. Epidemiological data shows the prevalence of GDM to be increasing. Strategies to prevent GDM are required and need to be evaluated such as the effects of advising on physical exercise (*Research Question 1*). Based on systematic reviews of the current literature, specific treatments for GDM are effective in improving pregnancy outcomes, although it is unclear exactly which type of diet is most effective in managing GDM (*Research Question 2*)

For women with intermediate forms of glucose intolerance without meeting current diagnostic criteria for GDM, the risk of adverse health outcomes is increased, but little is known about the effects of treatment during pregnancy on health outcomes for these women and their babies (*Research Question 3*) or the effects of the diagnosis on the women (Qualitative *Research Question 4*). Any treatment recommended for those women needs careful evaluation by high quality randomised controlled trials and systematic review of all relevant randomised controlled trials to assess the balance of benefits and harms of providing the proposed treatment, on maternal and infant health. Follow up beyond the postnatal period will be important (*Research Question 5*).

The research questions identified in this literature review form the basis for the research studies presented in this thesis (Table 1.7).

Table 1.7 Research questions addressed in the thesis of "Dietary and lifestyle advice for women to prevent and treat pregnancy hyperglycaemia: identifying and closing research gaps"

1	Can physical exercise for pregnant women reduce the risk of developing pregnancy glucose intolerance or gestational diabetes mellitus?
2	What are the effects of different types of dietary advice for women with GDM on pregnancy outcomes?
3	What are the effects of different types of management strategies for pregnant women with hyperglycaemia not meeting diagnostic criteria for GDM and T2DM?
4	What are women's experiences after being diagnosed with pregnancy hyperglycaemia without meeting GDM diagnostic criteria?
5	What are the effects of additional care including dietary and lifestyle advice compared with standard care for pregnant women with hyperglycaemia not meeting current diagnostic criteria for GDM on the health outcomes for women and their babies at four months after the birth?

2 Cochrane systematic review: Exercise for pregnant women for preventing gestational diabetes mellitus

This chapter includes a published Cochrane systematic review entitled “Exercise for pregnant women for preventing gestational diabetes mellitus”. An authorship statement including publication details has been attached on the next page.

2.1

Statement of Authorship

Title of Paper	Exercise for pregnant women for preventing gestational diabetes mellitus
Publication Status	◉ Published, ○ Accepted for Publication, ○ Submitted for Publication, ○ Publication style
Publication Details	Han S, Middleton P, Crowther CA. Exercise for pregnant women for preventing gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2012, Issue 7. Art. No.: CD009021. DOI: 10.1002/14651858.CD009021.pub2.

Author Contributions

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

Name of Principal Author (Candidate)	Shanshan Han		
Contribution to the Paper	Performed data extraction and assessment of risk of bias of the included studies; performed data analysis and data interpretation; wrote drafts of the protocol and review; acted as corresponding author.		
Signature		Date	31/3/14

Name of Co-Author	Philippa Middleton		
Contribution to the Paper	Performed data extraction and assessment of risk of bias of the included studies;contributed to data analysis and data interpretation; commented on and edited all drafts; supervised development and the progress of work.		
Signature		Date	27/3/14

Name of Co-Author	Caroline Crowther		
Contribution to the Paper	Contributed to data extraction, assessment of risk of bias of the included studies, data analysis and data interpretation; commented on and edited all drafts; supervised development and the progress of work.		
Signature		Date	19/3/14

Name of Co-Author			
Contribution to the Paper			
Signature		Date	

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

Han S, Middleton P, Crowther CA

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TABLE OF CONTENTS

[Intervention Review]

Exercise for pregnant women for preventing gestational diabetes mellitus

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ABSTRACT

Background

Gestational diabetes mellitus (GDM) affects a significant number of women each year. GDM is associated with a wide range of adverse outcomes for women and their babies. Recent observational studies have found physical activity during normal pregnancy decreases insulin resistance and therefore might help to decrease the risk of developing GDM.

Objectives

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

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (2 April 2012), ClinicalTrials.gov (2 April 2012) and the WOMBAT Perinatal Trials Registry (2 April 2012).

Selection criteria

Randomised and cluster-randomised trials assessing the effects of exercise for preventing pregnancy glucose intolerance or GDM.

Data collection and analysis

Two review authors independently assessed study eligibility, extracted data and assessed the risk of bias of included studies.

Main results

We included five trials with a total of 1115 women and their babies (922 women and their babies contributed outcome data). Four of the five included trials had small sample sizes with one large trial that recruited 855 women and babies. All five included trials had a moderate risk of bias. When comparing women receiving additional exercise interventions with those having routine antenatal care, there was no significant difference in GDM incidence (three trials, 826 women, risk ratio (RR) 1.10, 95% confidence interval (CI) 0.66 to 1.84), caesarean section (two trials, 934 women, RR 1.33, 95% CI 0.97 to 1.84) or operative vaginal birth (two trials, 934 women, RR 0.83, 95% CI 0.58 to 1.17). No trial reported the infant primary outcomes prespecified in the review.

None of the five included trials found significant differences in insulin sensitivity. Evidence from one single large trial suggested no significant difference in the incidence of developing pregnancy hyperglycaemia not meeting GDM diagnostic criteria, pre-eclampsia or admission to neonatal ward between the two study groups. Babies born to women receiving exercise interventions had a non-significant trend to a lower ponderal index (mean difference (MD) -0.08 gram x 100 m^3, 95% CI -0.18 to 0.02, one trial, 84 infants). No significant differences were seen between the two study groups for the outcomes of birthweight (two trials, 167 infants, MD -102.87 grams, 95% CI -235.34 to 29.60), macrosomia (two trials, 934 infants, RR 0.91, 95% CI 0.68 to 1.22), or small-for-gestational age (one trial, 84 infants, RR 1.05, 95% CI 0.25 to 4.40) or gestational age at birth (two trials, 167 infants, MD -0.04 weeks, 95% CI -0.37 to 0.29) or Apgar score less than seven at five minutes (two trials, 919 infants, RR 1.00, 95% CI 0.27 to 3.65). None of the trials reported long-term outcomes for women and their babies. No information was available on health services costs.

Authors' conclusions

There is limited randomised controlled trial evidence available on the effect of exercise during pregnancy for preventing pregnancy glucose intolerance or GDM. Results from three randomised trials with moderate risk of bias suggested no significant difference in GDM incidence between women receiving an additional exercise intervention and routine care.

Based on the limited data currently available, conclusive evidence is not available to guide practice. Larger, well-designed randomised trials, with standardised behavioural interventions are needed to assess the effects of exercise on preventing GDM and other adverse pregnancy outcomes including large-for-gestational age and perinatal mortality. Longer-term health outcomes for both women and their babies and health service costs should be included. Several such trials are in progress. We identified another seven trials which are ongoing and we will consider these for inclusion in the next update of this review.

PLAIN LANGUAGE SUMMARY

Exercise for pregnant women for preventing gestational diabetes mellitus

Each year, a significant number of pregnant women around the world develop gestational diabetes mellitus (GDM), defined as glucose intolerance or high blood glucose concentration (hyperglycaemia) with onset or first recognition during pregnancy. During normal pregnancy, insulin becomes less effective in transferring glucose from the blood stream to the mother's tissues to ensure an adequate nutrient supply to the baby. This insulin resistance increases as the pregnancy advances and GDM occurs when a mother does not secrete enough insulin to be able to meet this resistance. Women with GDM are at risk of future type 2 diabetes and their babies are at increased risk of adverse outcomes including being large-for-gestational age, having birthweight of at least 4000 grams and birth trauma. The modifiable risk factors for GDM include being overweight or obese; physical inactivity or sedentary lifestyle; low fibre and high glycaemic load diet and polycystic ovarian syndrome. This review aimed to assess the effects of physical exercise for pregnant women in preventing glucose intolerance or GDM and was based on limited evidence from five randomised controlled trials. Two trials involved obese women. The trials provided data from 922 women and their babies and were of moderate risk of bias. The exercise programs including individualised exercise with regular advice, weekly supervised group exercise session or home-based stationary cycling, either supervised or unsupervised, had no clear effect on preventing GDM (three trials with 826 women screened at 18 to 36 weeks' gestation), or improving insulin sensitivity (five trials) compared with standard antenatal care with normal daily activities. Based on these limited data, conclusive evidence is not available to guide practice. Larger, well-designed randomised trials are needed. Several such trials are in progress. We identified another seven trials which are ongoing and we will consider these for inclusion in the next update.

BACKGROUND

Description of the condition

Introduction and definition of gestational diabetes mellitus

Although there is no universally accepted diagnostic criteria (Coustan 2010), gestational diabetes mellitus (GDM) can be defined as 'glucose intolerance or hyperglycaemia (high blood glucose

concentration) with onset or first recognition during pregnancy' (ACOG 2001; Hoffman 1998; Metzger 1998; NICE 2008). GDM affects about 1% to 14% of pregnancies around the world and the prevalence is increasing in line with increasing rates of maternal obesity and type 2 diabetes mellitus (Bottalico 2007; Dabelea 2005; Mulla 2010).

Pathophysiology of gestational diabetes mellitus

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

Health risks for gestational diabetes mellitus

GDM is associated with a range of adverse pregnancy outcomes (Crowther 2005; HAPO Study Cooperative Research Group 2008; Landon 2009; Reece 2009).

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

As mentioned above, babies born to mothers with GDM are more likely to be LGA or macrosomic (HAPO Study Cooperative Research Group 2008; Ju 2008; Reece 2009). LGA or macrosomic infants are at increased risk of injury during birth, such as shoulder dystocia, perinatal asphyxia, bone fractures and nerve palsies (HAPO Study Cooperative Research Group 2008; Henriksen 2008; Langer 2005). Babies of women with GDM are also at higher risk of having other neonatal complications such as respiratory distress syndrome, hypoglycaemia, hyperbilirubinaemia (increased levels of bilirubin in the blood), cardiomyopathy (the deterioration of the function of the heart muscle layer), hypocalcaemia, hypomagnesaemia, polycythaemia, hyperviscosity and need admission to neonatal nursery (HAPO Study Cooperative Research Group 2008; Ju 2008; Reece 2009; Soler 1978). In the longer term, children born to mothers with GDM are at increased risk of becoming overweight or obese, developing type 1 and T2DM and having impaired intellectual achievement (Harder 2009; Mulla 2010; Rizzo 1997; Whincup 2008; Yogev 2009). Infants born LGA have a higher risk of developing metabolic syndrome (a cluster of risk factors defined by the occurrence of three of the following: obesity, hypertension, hypertriglyceridaemia and low HDL cholesterol concentration) in childhood, adolescence and adulthood (Barker 1994; Guerrero-Romero 2010; Harder 2009). Development of the metabolic syndrome during childhood predicts adulthood T2DM at 25 to 30 years of age (Morrison 2008). These health problems may repeat across generations (Mulla 2010; Petitt 1985).

Risk factors for GDM

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

Management of GDM

The primary aims of treatment for GDM are to optimise glycaemic control and improve pregnancy outcomes (Alwan 2009). Management for women with GDM is effective in improving pregnancy outcomes, which includes any or all of: diet and lifestyle advice, use of oral glucose-lowering agents (e.g. metformin, glyburide), administration of insulin, fetal surveillance (e.g. doppler umbilical blood flow measurement, cardiotocograph and ultrasonography) and maternal glucose monitoring (Crowther 2005; Hoffman 1998; Landon 2009; Metzger 2007; NICE 2008).

Dietary and lifestyle advice is effective (Crowther 2005; Landon 2009) and is usually recommended as the primary therapeutic strategy for women with GDM to achieve acceptable glycaemic control (ACOG 2001; Hoffman 1998; NICE 2008). As part of the treatment for GDM, women are encouraged to start or continue moderate intensity exercise as long as they have no medical or obstetrical contraindications (ADA 2003; Hoffman 1998; NICE 2008). If these interventions alone are not enough to achieve

good maternal glycaemia control, insulin therapy may be indicated (ACOG 2001; Hoffman 1998; NICE 2008). Oral hypoglycaemics such as glyburide and metformin have been used as alternatives to insulin therapy (Silva 2010; Simmons 2004). As part of management of GDM, maternal glucose monitoring and ultrasonography are advised to monitor treatment and guide care for birth (ACOG 2001; Hoffman 1998; NICE 2008).

Description of the intervention

Physical activity and pregnancy

Until several decades ago, physical activity had been discouraged in pregnancy due to theoretical concerns of exercise-induced injury leading to adverse fetal and maternal outcomes (Dempsey 2005; Schlüssel 2008).

Since early this century, the benefits of exercise during pregnancy have been realised and pregnant women have been encouraged to have regular physical activity in the absence of medical or obstetric complications (Dempsey 2005; Schlüssel 2008). Light to moderate physical activity during a normal pregnancy provides various benefits for the mother and her fetus (Melzer 2010). For mothers, it helps reduce and prevent lower back pain, decreases fluid retention, reduces cardiovascular stress, increases oxygenation capacity and decreases blood pressure (Melzer 2010; Schlüssel 2008). Fetal benefits include decreased fat mass, reduced risk of being a LGA fetus, improved stress tolerance, and advanced neurobehavioural maturation (Melzer 2010; Snapp 2008). Recent observational studies have found physical activity during normal pregnancy decreased insulin resistance and therefore, might help to decrease the risk of GDM (Redden 2010; Reece 2009). Some evidence from observational studies has suggested that the risk of GDM was decreased by 20% to 55% among women with physical exercise of various duration and intensity before or during pregnancy (Dempsey 2004a; Dempsey 2004b; Oken 2006; Zhang 2006).

How the intervention might work

Undertaking a period of exercise and regular weight-bearing exercise have both been found to decrease circulating glucose and insulin concentrations during, and for a period of time after, exercise sessions (Clapp 1991; Clapp 1998). The effect was greatest with low-intensity prolonged exercise that utilises a large muscle mass in late pregnancy shortly (less than two hours) after food intake (Clapp 2006). Investigators have shown that physical exercise was effective in preventing and managing T2DM by reducing insulin resistance in men and non-pregnant women (Clapp 2006; Knowler 2002; Oken 2006; Redden 2010). Regular exercise during pregnancy is associated with decreased circulating TNF-α levels in a dose- and time-dependent manner (Clapp 2000). These research findings suggest that physical exercise during normal pregnancy may be effective in preventing GDM.

In addition, being overweight or obese, or gaining excessive weight during pregnancy are significant risk factors for developing GDM (Hedderson 2010; Kim 2010b). A recent systematic review suggested physical activity during pregnancy might be successful in restricting gestational weight gain (Streuling 2011), thereby reducing the risk of developing GDM. However, such benefit was not found in another Cochrane review entitled '*Aerobic exercise for women during pregnancy*', aimed at assessing the effects of exercise for healthy pregnant women (Kramer 2006).

Why it is important to do this review

GDM affects a significant proportion of pregnant women each year and the prevalence is increasing worldwide (Bottalico 2007; Dabelea 2005; Mulla 2010). GDM is associated with a range of negative pregnancy outcomes and these adverse health outcomes can repeat across generations (HAPO Study Cooperative Research Group 2008; Mulla 2010). Therefore, identifying ways that might help prevent GDM is of urgent public health importance.

Although the risk factors and health outcomes of GDM have been well recognised, there is little known about ways to prevent GDM in high-risk populations (Mottola 2008; Petry 2010; Pivarnik 2006). Physical exercise, as one of the modifiable risk factors for GDM, has attracted great attention in recent years (Melzer 2010). There has been a suggestion that physical exercise before and during pregnancy may be effective in preventing GDM; however, little robust evidence from randomised controlled trials is available (Petry 2010). This review will help to provide reliable evidence for pregnant women on the effects of physical exercise on GDM prevention. Three other Cochrane reviews have addressed the effects of exercise for diabetic pregnant women (Ceysens 2006), the role of aerobic exercise for healthy pregnant women (Kramer 2006) and the effects of diet and exercise on postpartum weight retention (Amorim 2007). Another Cochrane review to assess the effects of combined diet and exercise for preventing GDM is being planned.

OBJECTIVES

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

METHODS

Criteria for considering studies for this review

Types of studies

All published randomised controlled trials assessing the effects of physical exercise in preventing pregnancy glucose intolerance or GDM. We planned to include cluster-randomised trials. We also planned to include published abstracts for randomised controlled trials and cluster-randomised controlled trials when relevant outcome data were available. We excluded quasi-randomised controlled trials and cross-over trials.

We planned to include trials assessing the effects of lifestyle interventions (e.g. include both nutrition and physical exercise interventions) in preventing pregnancy glucose intolerance or GDM if we are able to extract data for the effects of physical exercise separately.

Types of participants

Pregnant women regardless of age, gestation, parity or plurality. We excluded women with pre-existing type 1 and type 2 diabetes.

Types of interventions

Interventions included any types of exercise and lifestyle management (i.e. exercise advice, providing exercise sessions) for pregnant women for preventing GDM before screening tests.

One type of intervention would be compared to standard antenatal care, i.e. any type of exercise advice (standard advice or individualised advice) compared with standard antenatal care; providing exercise sessions (group exercise or individual exercise session) compared with standard care. Multiple form of interventions would be compared with standard care, i.e. providing exercise advice and exercise sessions compared with standard care. Two forms of interventions would be compared with each other, i.e. providing exercise advice compared with providing exercise session. Two or more types of the same form of management would be compared against each other, i.e. standard exercise advice compared with individualised exercise advice; group exercise session compared with individual exercise session; different intensities of exercise sessions compared with each other; exercise interventions only compared with exercise interventions plus other forms of intervention (e.g. providing dietary advice).

Types of outcome measures

Primary outcomes

Maternal outcomes

1. Incidence of GDM (diagnostic criteria as defined in individual trials)
2. Mode of birth (normal vaginal birth, operative vaginal birth, caesarean section)

Fetal/neonatal outcomes

1. LGA
2. Perinatal mortality (fetal and neonatal mortality)

Secondary outcomes

Maternal outcomes

Perinatal

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

Long term

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

Fetal/neonatal outcomes

1. Macrosomia (birthweight at least 4000 g)
2. Birthweight
3. Small-for-gestational age
4. Neonatal hypoglycaemia requiring treatment (variously defined by authors of individual trials)
5. Gestational age at birth
6. Preterm birth (less than 37 weeks' gestation)
7. Shoulder dystocia
8. Bone fracture

9. Nerve palsy
10. Respiratory distress syndrome
11. Hyperbilirubinaemia requiring treatment (variously defined by authors of individual trials)
12. Apgar scores (less than seven at five minutes)
13. Ponderal index
14. Skinfold thickness measurements

Childhood outcomes

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

Adulthood outcomes

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

Health services cost

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

Search methods for identification of studies

Electronic searches

We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (2 April 2012).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

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

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

Searching other resources

We searched the reference lists of retrieved articles and reviewed the list of perinatal trials included in the Women and Babies Health and Wellbeing: Action through Trials (WOMBAT) Perinatal Trials Registry (WOMBAT) (2 April 2012). We also searched the ClinicalTrials.gov trial registry (2 April 2012) to identify potential relevant trials. The search strategy used is included in Appendix 1. We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Two review authors independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We resolved any disagreement through discussion or, if required, we consulted a third person.

Data extraction and management

We designed a form to extract data. For eligible studies, at least two review authors extracted the data using the agreed form. We resolved discrepancies through discussion or, if required, we consulted a third person. We entered data into Review Manager software (RevMan 2011) and checked for accuracy.

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (*Handbook*) (Higgins 2011). We resolved any disagreement by discussion or by involving a third assessor.

(1) Sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We 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 each included study the method used to conceal the allocation sequence and determine whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We 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 describe for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We 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 each included study the methods used, if any, 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 through withdrawals, dropouts, protocol deviations)

We described for each 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, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we re-included 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 bias

We described for each 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 was clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review had been reported);
- high risk of bias (where not all the study's pre-specified outcomes had been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest were reported incompletely and so could not 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 sources of bias

We described for each included study any important concerns we had about other possible sources of bias.

We assessed whether each 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.

(7) Overall risk of bias

We made explicit judgements about whether studies were 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 we considered it was likely to impact on the findings. We planned to explore the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

Measures of treatment effect

Dichotomous data

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

Continuous data

For continuous data, we used the mean difference when outcomes were measured in the same way between trials. If necessary, we would have used the standardised mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials

We did not identify any cluster-randomised trials for inclusion. In future updates of this review, if we identify cluster-randomised trials, we plan to include them in the analyses along with individually-randomised trials. We will adjust their sample sizes using the methods described in the *Handbook* using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population (Higgins 2011). If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely.

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

Dealing with missing data

For included studies, we noted levels of attrition. We explored the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis. For all outcomes, we 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 was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the T^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if I^2 was greater than 30% and either T^2 was greater than zero, or there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

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

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2011). We used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar. If there had been clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity had been detected, we planned to use random-effects

meta-analysis to produce an overall summary if an average treatment effect across trials was considered clinically meaningful. The random-effects summary would have been treated as the average range of possible treatment effects and we would have discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we would not have combined trials.
If we had used random-effects analyses, we would have presented the results as the average treatment effect with its 95% confidence interval, and the estimates of T^2 and I^2.

Subgroup analysis and investigation of heterogeneity

If we had identified substantial heterogeneity, we would have investigated it using subgroup analyses and sensitivity analyses. We planned to consider whether an overall summary was meaningful, and if it was, use random-effects analysis.
Maternal characteristics, and characteristics of exercise interventions might affect health outcomes. We planned to carry out the following subgroup analyses, but there were not enough trials providing relevant data to conduct these subgroup analyses.

1. Maternal characteristics

- Maternal age:
  - we planned to compare women of 35 years of age or more with women less than 35 years of age.
- Maternal body mass index (BMI) (at or before trial entry):
  - we planned to compare women with BMI ranges of 18.5 to 24.9 kg/m² with those with less than 18.5 kg/m²;
  - BMI ranges of 18.5 to 24.9 kg/m² with those of 25 to 29.9 kg/m²;
  - BMI ranges of 18.5 to 24.9 kg/m² with those of 30 kg/m² to 39.9 kg/m²;
  - BMI ranges of 18.5 to 24.9 kg/m² with those of 40 kg/m² or more.
- Ethnicity:
  - we planned to compare high-risk ethnic groups with low-risk ethnic groups.
- Parity:
  - we planned to compare parity of zero with one to two;
  - parity of zero with three or more.

2. Nature of exercise interventions

- Exercise intervention only compared with exercise intervention plus other forms of intervention (e.g. dietary advice).
- Frequency of the intervention:
  - we compared frequencies of one to four times/week with five or more times/week.
- Duration of the intervention:
  - we planned to compare less than 20 minutes per session with 20 minutes or more per session.
- Intensity of the exercise sessions:*
  - we planned to compare light intensity exercise with moderate intensity exercise;
  - we planned to compare light intensity exercise with high intensity exercise.

*intensity of exercise was defined by individual trials.

3. Ways of delivering intervention

We planned to compare:
- exercise advice only with providing exercise sessions;
- face-to-face intervention with non-face-to-face intervention (e.g. phone counselling, information package, etc.);
- group intervention with individual intervention.

We planned to use primary outcomes in subgroup analyses.
We planned to assess differences between subgroups by interaction tests where possible.

Sensitivity analysis

In future updates of this review, we plan to carry out sensitivity analysis to explore the effects of trial quality assessed by allocation concealment and other risk of bias components, by omitting studies rated as 'high risk of bias' for these components. Sensitivity analysis will be restricted to the primary outcomes.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search

A total of 22 trials were identified for consideration of inclusion in this review. Nineteen trials were identified through the search conducted by the Cochrane Pregnancy and Childbirth Group and three additional trials were identified through searching ClinicalTrials.gov (ClinicalTrials 2011) and the WOMBAT (Women and Babies health and wellbeing: Action through Trials) Perinatal Trials Registry (WOMBAT 2011).

Following application of the eligibility criteria for the review, we included five trials (Barakat 2011; Callaway 2010; Hopkins 2010; Ong 2009; Stafne 2012). Ten trials did not meet the inclusion criteria for this review and were excluded (Chen 1997; Clapp 1997; Clapp 2002; Clapp 2002a; Gaston 2009; Haakstad 2011; Hui 2006; Kim 2010a; Luoto 2010; Quinlivan 2007). Another seven trials (Chasan-Taber 2009; Ko 2008; Melo 2008; Newnham 2011; Oostdam 2009; Ramirez-Velez 2009; Shen 2008) are ongoing and will be considered for inclusion in the next update of this review (*see* Characteristics of ongoing studies).

Included studies

For full details, *see* Characteristics of included studies.

Two of the five included trials (Callaway 2010; Ong 2009) were conducted in Australia, One trial each was conducted in New Zealand (Hopkins 2010), Spain (Barakat 2011) and Norway (Stafne 2012).

Participants

A total of 1115 women and their babies were recruited in the five included trials and 922 women and their babies were involved in the data analysis. Four included trials had small sample sizes (Barakat 2011; Callaway 2010; Hopkins 2010; Ong 2009) and one trial (Stafne 2012) randomised 855 women.

In Callaway 2010 and Ong 2009 only obese (body mass index (BMI) greater or equal to 30 kg/m²) women were included. In Barakat 2011, women had a mean [SD] pre-pregnancy BMI of 22.7 [2.8] kg/m² in the intervention group and 23 [2.9] kg/m² in the control group. Hopkins 2010 included healthy nulliparous women with a mean BMI [SD] of 25 [4] kg/m² at trial entry (mean trial entry gestational age [SD]: 19 [1.1] weeks). In Stafne 2012, women in the intervention group had a trial entry mean BMI [SD] of 24.7 [3.0] kg/m² and 25.0 [3.4] kg/m² for women in the control group (women at trial entry were at around 18 weeks' gestation).

Intervention and comparison

In Barakat 2011, women in the intervention group received 35-45-minutes supervised sessions three times a week with two land aerobic sessions and one aquatic activities session. In Callaway 2010, an individualised exercise plan with an energy expenditure goal of 900 kcal per week was provided to women in the intervention group. Other interventions in this trial included four-weekly follow-up for assessment of adherence and diaries for self-monitoring (Callaway 2010). In Hopkins 2010, interventions were home-based stationary cycling for a maximum of five sessions of 40 minutes aerobic exercise per week, for the remaining weeks of pregnancy. This aimed for a moderate intensity of 65% of predicted aerobic capacity (VO_{2max}). In addition, women had fortnightly supervised sessions, reviewing their exercise plan and checking for adherence (Hopkins 2010). In Ong 2009, women had home-based supervised stationary cycling for three sessions a week over a 10-week period (between 18 weeks of gestation and 28 weeks of gestation). During each session, women had a 10-minute warm-up followed by one or two 15-minute bouts of cycling at an intensity of 50 to 60% $HR_{max.}$ and the exercise intensity was increased to 60 to 70% HR_{max} as pregnancy progressed (Ong 2009). In Stafne 2012, women had a weekly supervised 60-minute group exercise session at moderate to high intensities for a period of 12 weeks. Women were also encouraged to follow a written 45-minute home exercise program at least twice per week (Stafne 2012).

In four included trials , women in the control group had standard antenatal care with normal daily activities (Callaway 2010; Hopkins 2010; Ong 2009; Stafne 2012). One included trial did not provide information on what type of care was provided for women in the control group (Barakat 2011).

See Characteristics of included studies table for more details.

Outcome

All the five included trials focused on perinatal outcomes for women and their babies (Barakat 2011; Callaway 2010; Hopkins 2010; Ong 2009; Stafne 2012). None of the included studies have reported any longer-term outcomes as yet for mothers or their children.

See Characteristics of included studies for more details.

Excluded studies

Of the 10 excluded trials, three trials were excluded due to their interventions not meeting the inclusion criteria specified for the review (Clapp 2002; Gaston 2009; Quinlivan 2007). In Clapp 2002, all participants received the same exercise intervention but different dietary interventions; Gaston 2009 aimed to assess whether maternal-fetal disease information was a good source of exercise motivation during pregnancy with no clinically relevant outcomes reported in their paper; and in Quinlivan 2007, exercise was not a part of the study intervention. Another two trials (Hui 2006; Luoto 2010) were excluded as interventions in these two trials included both exercise and diet, and data on the effect of exercise were not able to be abstracted separately. Clapp 2002a and Haakstad 2011 were excluded due to no relevant data reported on pregnancy glucose tolerance. Chen 1997 and Kim 2010a were excluded due to participants not meeting the inclusion criteria of this review and Clapp 1997 was a literature review, not a report of a trial.

See Characteristics of excluded studies for more details.

Risk of bias in included studies

We judged the five included trials to have a moderate risk of bias overall. *See* Figure 1 and Figure 2.

Figure 1. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

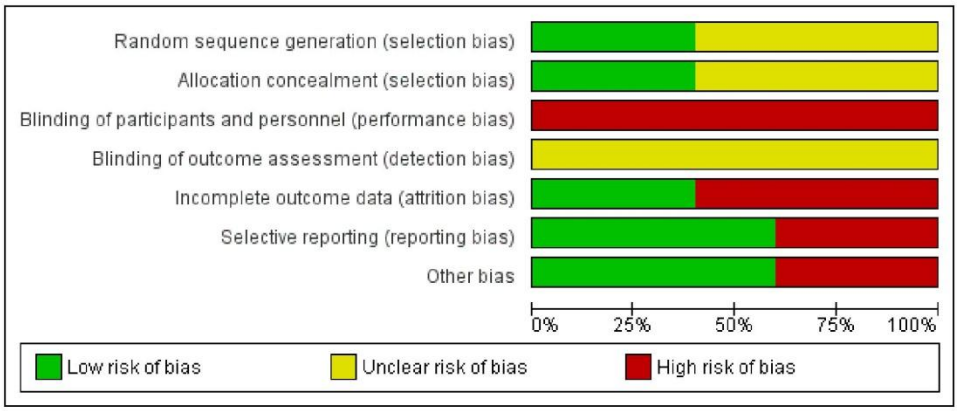
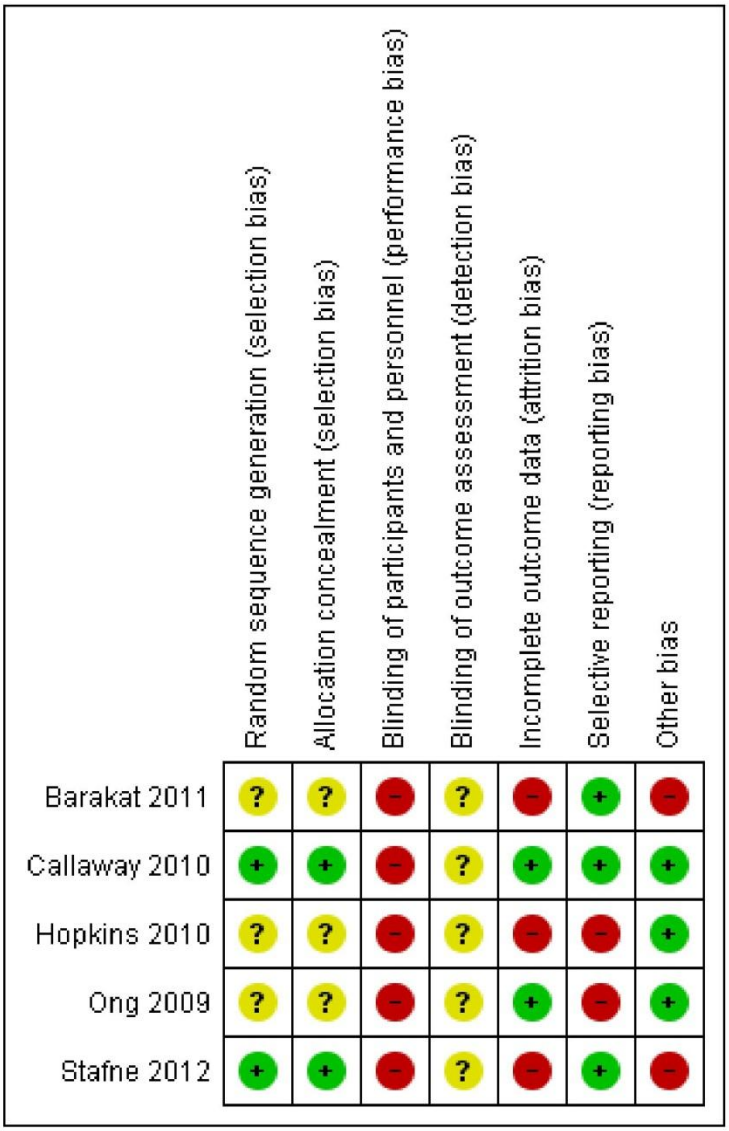


Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



Random sequence generation (selection bias)

Three of the five included trials reported women were randomly allocated to study groups without further details being provided (Barakat 2011; Hopkins 2010; Ong 2009). In Callaway 2010, a random number allocation technique was applied for randomisation and Stafne 2012 performed by a web-based computerised procedure in blocks of 30.

Allocation

In Callaway 2010 and Stafne 2012, randomisation was conducted by a third party at another location outside the hospital. The other three included trials had no information on allocation concealment (Barakat 2011; Hopkins 2010; Ong 2009).

Blinding

It was unclear whether outcome assessors were blinded to group allocation in all of the five included trials (Barakat 2011; Callaway 2010; Hopkins 2010; Ong 2009; Stafne 2012). Participants in the five trials were not blinded.

Incomplete outcome data

In Barakat 2011, 10/50 (20%) women from the exercise group and 7/50 (14%) women from the control group did not complete the study and were excluded from the analysis. Reasons for exclusion included developing medical complications and personal reasons such as change of residence (Barakat 2011).

In Callaway 2010, five (10%) women in the intervention group and nine (18%) women in the control group were lost to follow-up by six weeks postpartum. Of the 14 women lost to follow-up in this study, two (4%) in the intervention group and three (6%) in the control were not able to be contacted; three (6%) in the intervention group and six (12%) women in the control group were lost to follow-up as they met the prespecified criteria to terminate the intervention (Callaway 2010). These criteria included persistent second and third trimester bleeding, placenta praevia after 26 weeks' gestation, preterm labour, ruptured membranes, and pre-eclampsia (Callaway 2010).

For Hopkins 2010, a total of 14 (14.3%) women were lost to follow-up. Eleven women withdrew from study two (2.4%) in the intervention group and nine (10.7%) women in the control group. Another three (3.6%) women in the control group were lost to follow-up due to development of contraindications to exercise.

In Stafne 2012, 7.7% (33/429) women in the exercise group and 14.3% (61/426) women in the control group were lost to follow-up during pregnancy and another 5.3% (21/396) women in the intervention group and 10.4% (38/365) women in the control group were excluded at 32 to 36 weeks assessment. Reported reasons for exclusion included developing medical complications, change of residence, did not attended oral glucose tolerance test (OGTT) or did not attend hospital interview (Stafne 2012).

No losses to follow-up or post randomisation exclusions were reported in Ong 2009.

Selective reporting

Two included trials did not report any of the prespecified primary outcomes of this review including GDM incidence (Hopkins 2010; Ong 2009). There was no obvious risk of selective reporting in Barakat 2011, Callaway 2010 and Stafne 2012.

Other potential sources of bias

In Barakat 2011, baseline characteristics were only reported for women who completed the study. Among women who completed the study, there was baseline imbalance in maternal education level, parity and exercise habits before gestation between the two study groups (Barakat 2011).

In Stafne 2012, baseline imbalance existed in insulin resistance between women in the exercise group and the control group. Women in the intervention group had lower insulin resistance at baseline when compared with women in the control group. It was also reported that among women who completed the study, those in the intervention group had lower fasting insulin and insulin resistance than women in the control group. Women lost to follow-up in Stafne 2012 performed exercise less often before pregnancy than those who completed the study.

There was no obvious risk of other potential sources of bias in the other four included trials (Barakat 2011; Callaway 2010; Hopkins 2010; Ong 2009).

Effects of interventions

Any additional exercise intervention versus routine antenatal care only

Primary outcomes

Three trials reported GDM incidence (Barakat 2011; Callaway 2010; Stafne 2012). In Barakat 2011 and Callaway 2010, GDM was screened at 24 to 28 weeks' gestation and women in Stafne 2012 were screened for GDM at both baseline (between 18 to 22 weeks' gestation) and the end of the intervention period (between 32 to 36 weeks' gestation). Three different GDM diagnostic criteria, including American Diabetes Association (ADA) criteria, Australasian Diabetes in Pregnancy Society (ADIPS) criteria and

the WHO criteria were used in the three trials (Barakat 2011; Callaway 2010; Stafne 2012).

No significant difference was seen in the GDM incidence between women receiving additional exercise intervention and those having routine antenatal care (three trials, 826 women, risk ratio (RR) 1.10, 95% confidence interval (CI) 0.66 to 1.84) (Analysis 1.1).

Women receiving exercise interventions had a slightly increased caesarean section rate, however, the difference was only of borderline significance (two trials, 934 women, RR 1.33, 95% CI 0.97 to 1.84) (Analysis 1.2). No significant difference was seen in the rate of operative vaginal birth between women in the exercise group and control group (two trials, 934 women, RR 0.83, 95% CI 0.58 to 1.17) (Analysis 1.3).

No trial reported large-for-gestational age and perinatal mortality.

Secondary outcomes

Maternal outcomes

There was no significant difference in the incidence of women developing pregnancy hyperglycaemia not meeting GDM diagnostic criteria (one trial, 83 women, RR1.07, 95% CI 0.16 to 7.27) (Analysis 1.4). Women receiving the additional exercise intervention had no significant differences in weight in late pregnancy (one trial, 84 women, mean difference (MD) - 1.10 kg, 95% CI - 6.11 to 3.91), weight gain during the intervention period (exercise interventions lasted for less than one trimester) (one trial, 12 women, MD - 1.50 kg, 95% CI - 4.41 to 1.41) or weight gain during the intervention period (exercise interventions lasted for one trimester or more) (one trial, 83 women, MD -1.30 kg, 95% CI -2.66 to 0.06) when compared with women having routine care (Analysis 1.5). For maternal BMI in late pregnancy, data from one trial (Hopkins 2010) suggested no significant difference between the two study groups (84 women, MD 0.10 kg/m^{2}, 95% CI - 1.39 to 1.59) (Analysis 1.6). No significant difference was seen in the incidence of pre-eclampsia between women in the exercise intervention group and the control group (one trial, 852 women, RR 1.00, 95% CI 0.51to 1.97) (Analysis 1.7).

Adherence to the exercise intervention was reported as excellent in four of the five included trials (Barakat 2011, Callaway 2010; Hopkins 2010; Ong 2009). Barakat 2011 reported 85% of women in the intervention group adhered to the exercise intervention without providing information on the definition of adherence. In Callaway 2010, 15 women (71%) achieved the prescribed exercise goal at 20 weeks' gestation, 16 women (73%) at 28 weeks' gestation and 10 women (53%) at 36 weeks' gestation. In Hopkins 2010, women in the intervention group completed 75% [SD] 17% of total exercise prescribed. In Ong 2009, 94% of all scheduled exercise sessions were completed by women in the intervention group. In Stafne 2012, 55% (n = 217) women in the intervention group were adherent, which was defined as exercising three days per week or more at moderate to high intensity, while10% (n = 33) women in the control group were found to be exercising three days per week or more at moderate to high intensity during the study period.

Insulin sensitivity was reported in four trials (Callaway 2010; Hopkins 2010; Ong 2009; Stafne 2012). Different methods and different time points were chosen to measure insulin sensitivity in the four trials, so it was not possible to statistically combine these results. In Stafne 2012 and Callaway 2010, insulin resistance was estimated using "Homeostasis model" (HOMA-IR). Stafne 2012 found a significant lower insulin resistance in women receiving the exercise intervention at 32 to 36 weeks' gestation when compared with women in the control group, however, this difference became non-significant after adjusting for baseline imbalance in insulin resistance between the two study groups. Callaway 2010 found no significant difference in insulin sensitivity at 12 weeks, 20 weeks, 28 weeks and 36 weeks' gestation between women receiving the additional exercise intervention and those having routine antenatal care. Hopkins 2010 used minimal model analysis of parameters of insulin sensitivity. MINMOD Millennium computer program was used to calculate insulin sensitivity index, acute insulin response, glucose effectiveness based fasting insulin and glucose values. No difference was seen in any parameters of glucose regulation during pregnancy between women in the exercise intervention group and control group at trial entry (19+/- 1.1 weeks' gestation) or late pregnancy (35+/-0.8 weeks' gestation) (Hopkins 2010). In Ong 2009, insulin sensitivity was determined from the OGTT using a validated oral glucose insulin sensitivity (OGIS) index and reported no significant difference between women in the two study groups at 28 weeks' gestation.

There were no data available on other maternal perinatal outcomes and no trial reported longer-term outcomes and health services cost.

Fetal/neonatal outcomes

For fetal and neonatal secondary outcomes, no significant difference was found between babies born to women in the exercise intervention group and control group for birthweight (two trials, 167 infants, MD -102.87 gram, 95% CI -235.34 to 29.60) (Analysis 1.8); macrosomia (two trials, 934 infants, RR 0.91, 95% CI 0.68 to 1.22) (Analysis 1.9); small-for-gestational age (one trial, 84 infants, RR 1.05, 95% CI 0.25 to 4.40) (Analysis 1.10); or gestational age at birth (two trials, 167 infants, MD -0.04 week; 95% CI -0.37 to 0.29) (Analysis 1.11). Babies born to women receiving exercise interventions had a slightly lower ponderal index, however, the difference was only of borderline significance (one trial, 84 infants, MD -0.08 gram x 100/m^{3}, 95% CI -0.18 to 0.02) (Analysis 1.12). No significant differences were seen in the incidences of Apgar score less than seven in five minutes (two trials, 919 infants, RR 1.00, 95% CI 0.27 to 3.65) (Analysis 1.13) and admission to neonatal ward (one trial, 838 infants, RR 0.77, 95%

CI 0.39 to 1.53) (Analysis 1.14) between the two study groups. There were no data available on the other neonatal and infant review outcomes. No trial has reported on childhood or adulthood outcomes and health services cost.

DISCUSSION

Summary of main results

Based on the current available evidence from five randomised trials with data available from 992 women and their babies, we found exercise interventions, including individualised exercise advice with regular follow-up, home-based stationary cycling either supervised or unsupervised, or providing regular supervised group exercise sessions had no significant effect on preventing gestational diabetes mellitus (GDM) or improving insulin sensitivity during pregnancy compared with standard antenatal care with normal daily activities.

We found women who received the exercise intervention had a trend of increased caesarean section rate, although the difference was only of borderline significance. This may result from the inclusion of outcome data from Barakat 2011, which found a doubled risk of caesarean section in women receiving exercise intervention. This increased risk for women in the exercise group in Barakat 2011 may result from the baseline imbalance in parity, where more women in the exercise group were primiparous when compared with women in the control group. Another possible explanation for this increased risk of caesarean section is the closer monitoring of women in the exercise group during the study period.

We did not find any significant differences in operative vaginal birth between women receiving additional exercise intervention and routine care. No significant differences were seen in any of the other reported maternal and infant secondary outcomes between the two study groups.

Overall completeness and applicability of evidence

The evidence for exercise during pregnancy for GDM prevention is incomplete. No trial reported on the primary outcomes for the review of large-for-gestational age and perinatal mortality.

Many reported secondary outcomes, including pregnancy hyperglycaemia not meeting GDM diagnostic criteria, maternal weight change during pregnancy, maternal BMI at late pregnancy, small-for-gestational age, ponderal index, were limited to single trials with small sample sizes (Barakat 2011; Hopkins 2010). No trial reported any longer-term outcomes for the women and their children. It is important to note that all of the five included trials were conducted in high-income countries (two were in Australia, one each from in New Zealand, Norwary and Spain), hence it is limited for other settings.

Quality of the evidence

In this review, we included five trials with 922 women and their babies providing outcome data (Barakat 2011; Callaway 2010; Hopkins 2010; Ong 2009; Stafne 2012). Four of the five included trials had small sample sizes (Barakat 2011; Callaway 2010; Hopkins 2010; Ong 2009) and the overall risk of bias for the five included trials was judged to be moderate.

The methods of generating random sequence and allocation concealment were unclear in three trials (Barakat 2011; Hopkins 2010; Ong 2009). Risk of performance bias is not easy to avoid since behavioural interventions such as these cannot easily be blinded from participants or investigators. This was seen in Callaway 2010 and Stafne 2012 where it was noted that women in the control group voluntarily increased the amount of physical activity they undertook. Similarly, some attrition after randomisation is to be expected as some women will develop contraindications to exercise during their pregnancy. However, there was also attrition due to women being lost to follow-up, with a substantial differential between intervention and control groups in Hopkins 2010 and Stafne 2012.

In Barakat 2011 and Stafne 2012, baseline imbalances were noted in maternal education level, parity, exercise habits before gestation and insulin resistance between the two study groups.

Potential biases in the review process

The baseline physical activity levels of the women were unclear in three included trials (Callaway 2010; Hopkins 2010; Ong 2009). Barakat 2011 reported women's pre-pregnancy exercise pattern while Stafne 2012 reported women's exercise pattern at around 20 weeks' gestation. A potential source of bias may be introduced by the different activity levels of women at trial entry in the different studies.

We were not able to examine if publication bias was present due to the small number of trials included in this review. We will test if there is any publication bias by using funnel plots when additional eligible trials become available.

Agreements and disagreements with other studies or reviews

We found no significant difference in the risk of developing GDM when comparing women receiving additional exercise interventions during pregnancy with those having standard antenatal care. The four included trials which reported outcome data on insulin sensitivity, used different methods to assess insulin sensitivity and showed no difference in insulin sensitivity at different gestation

weeks between women in the two treatment groups. We did not see any differences between women and their babies in the two study groups for any of the other reported secondary outcomes.

Another Cochrane review (Kramer 2006) and one non-Cochrane systematic review (Streuling 2011) on the effect of exercise during pregnancy were identified through searching the literature. Kramer 2006 assessed the effect of exercise during pregnancy on physical fitness, the course of labour and delivery and other pregnancy outcomes. A total of 14 small trials involving 1014 healthy pregnant women, of moderate to high risk of bias were reviewed (Kramer 2006). Streuling 2011 aimed to assess the effect of physical activity during pregnancy on gestational weight gain; 12 trials of varying risk of bias, involving 906 healthy pregnant women were reviewed.

Neither review (Kramer 2006; Streuling 2011) reported on the effects of exercise on preventing pregnancy glucose intolerance. Both reviews (Kramer 2006; Streuling 2011) reported on maternal gestational weight gain, and this was the only outcome reported in Streuling 2011. Kramer 2006 found increasing exercise in sedentary women had no significant effect on total maternal gestational weight gain, which was consistent with our results; while Streuling 2011 reported significant lower gestational weight gain in women in the intervention group compared with control group (12 trials, 906 women, MD -0.61 kg, 95% CI -1.17 to -0.06). In a sensitivity analysis, by excluding three trials with high risk of bias, this difference remained significant (MD -0.93, 95% CI -1.35 to -0.50) (Streuling 2011). This difference may result from the inclusion of one trial which found a significant difference in gestational weight gain between women in the exercise group and the control group (Sedaghati 2007) in Streuling 2011, but not included in our review or in Kramer 2006.

For other pregnancy outcomes, Kramer 2006 found the exercise intervention had no significant effect on caesarean section rate, infant birthweight, and gestational age at birth, which was consistent with our results.

AUTHORS' CONCLUSIONS

Implications for practice

There is a limited and incomplete body of evidence from randomised trials assessing the effects of exercise for preventing gestational diabetes or glucose intolerance in pregnancy, which is insufficient to inform or guide practice.

Implications for research

Further well-designed trials with sufficient power to assess the effects of exercise for pregnant women on GDM prevention and other pregnancy outcomes are needed. Different types and intensities of exercise interventions should be compared in future trials. Outcomes such as longer-term health outcomes for women and their children and health service costs should be included.

ACKNOWLEDGEMENTS

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As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team) and the Group's Statistical Adviser.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Barakat 2011

Methods	Randomised controlled trial.
Participants	100 healthy women having uncomplicated and singleton pregnancies Exclusion criteria: • Women not planning to give birth in the research participating hospital and not being under medical follow-up throughout the entire pregnancy period. • Any type of absolute obstetric contraindication such as: ○ Active illness of the myocardium. ○ Heart insufficiency. ○ Rheumatic heart illness (type II or above). ○ Thrombophlebitis. ○ Recent pulmonary embolism (last 5 years). ○ Acquired infectious disease. ○ Cervical incompetence. ○ Multiple pregnancy. ○ Genital haemorrhage. ○ Premature breakage of the ovular membranes. ○ Retarded interuterine development. ○ Fetal macrosomia. ○ Serious blood disease. ○ Serious hypertension. ○ Absence of prenatal control. ○ Suspects of fetal suffering. ○ Risk of premature labour. ○ Prepregnant type 1 or 2 DM. Setting: Madrid, Spain.
Interventions	Women in the intervention group (50 women randomised, 40 women completed study) : • 35-45-minute session performed 3 times a week with 2 land aerobic sessions and 1 aquatic activities session, from the start of the pregnancy (weeks 6-9) to the end of the third trimester (weeks 38-39). A total of 85 sessions were planned for each women if not having a preterm delivery. • Exercise sessions were supervised by a qualified fitness specialist and obstetrician. • HR monitor was used during the training sessions to ensure that exercise intensity was light to moderate (HR was consistently under 70% of their age predicted maximum HR value (220 minus age)). Women in the control group (50 women randomised, 43 women completed study): • No information reported on what type of care provided for women in the control group.
Outcomes	Primary: 50 g maternal glucose screen, maternal weight gain and GDM Secondary: maternal age, BMI, smoking habits, alcohol intake, occupational activity, time standing per day, time of domestic task, educational level, parity, gestational age,

	type of delivery, blood pressure, birthweight, Apgar score and adherence (women in the intervention group)
Notes	• All women had 50 g maternal glucose screening (MGS) test at 24-28 weeks' gestation. If 50 g result > 140 mg/dL (7.8mmol/L), women were referred for a 100-g 3-h OGTT. • GDM diagnosis based on ADA criteria: ○ Fasting: 95 (5.3mmol/L) ○ 1-hour BGL after 100 g glucose load: 180 (10.0 mmol/L) ○ 2-hour BGL after 100 g glucose load: 155 (8.6 mmol/L) ○ 3-h BGL after 100 g glucose load: 140 (7.8 mmol/L) ○ 2 or more of the values must be met or exceeded.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Stated as "women were randomly assigned either to an exercise group or a control group"
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information reported on whether outcome assessors were blinded to group allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	10/50 (20%) women from the exercise group did not complete study, reported reasons were: risk of premature labour (n = 3), incompetent cervix was diagnosed (n = 2) and personal reasons such as change of residence (n = 5) 7/50 (14%) participants of the control group did not complete study, reported reasons were: pregnancy-induced hypertension (n = 1), risk for premature labour (n = 2) and personal reasons (n = 4)
Selective reporting (reporting bias)	Low risk	No obvious risk of selective reporting.
Other bias	High risk	Baseline characteristics were only available for women who completed study (83/100) Among the women who completed study, baseline imbalance exited in maternal education level, parity and exercise habits before gestation between the two study groups

Callaway 2010

Methods	Randomised controlled trial.
Participants	50 obese women (BMI $\geq$ 30 kg/m²) aged 18-45 years, who were willing and able to be randomised to an exercise intervention Exclusion criteria: non-English speaking, contraindication or inability to exercise, medical or obstetric contraindication to exercise including haemodynamically significant heart disease, restrictive lung disease, incompetent cervix (cerclage), multiple gestation, severe anaemia, chronic bronchitis, type 1 diabetes, orthopaedic limitations, poorly controlled seizure disorder, poorly controlled hyperthyroidism, or a heavy smoker Setting: the Royal Brisbane and Women's Hospital (a tertiary referral teaching hospital) , Queensland, Australia
Interventions	• Women in the intervention group (n = 25) 1. An individualised exercise plan with an energy expenditure goal of 900 kcal/ week: a physiotherapist interviewed women at around 12 weeks' gestation to develop women's individualised exercise plans to suit each woman's lifestyle. During the interview, women were encouraged to set exercise goals and their readiness for change was assessed. 2. Regular exercise advice: women were reviewed every 4 weeks by physiotherapists, with phone calls between visits from a research midwife to assess their adherence to the program. Modifications to exercise were made according to women's interest, commitment to particular exercise options and for weather. A total of 6 face-to-face visits were planned during the trial, and on average women attended for 4. 3. Paper-based diaries for self-monitoring. 4. Women who were not meeting exercise targets had additional face-to-face support, with identification of barriers and modification of the exercise plan. • Women in the control group (n = 25) 1. Routine obstetric care. • All women 1. At pre-intervention stage, all eligible women were invited to attend a single early group education session at around 12 weeks' gestation. Women received written information on exercise, nutrition, and advice regarding weight gain during pregnancy.
Outcomes	Primary outcomes: energy expenditure at 12, 20, 28 and 36 weeks' gestation; insulin resistance at 12, 20, 28 and 36 weeks' gestation Other outcomes: gestational diabetes mellitus (according to ADIPS criteria (*see* notes)).
Notes	• Women in the control group voluntarily undertook far more physical activity than predicted. • At 12 weeks' gestation, 10/25 (40%) women in the intervention group and 7/25 (28%) women in the control group met the exercise goal of greater than 900 Kcal energy expenditure per week. • At 20 weeks' gestation, 15/21 (71%) women in the intervention group and 9/19 (47%) women in the control group met the exercise goal of greater than 900 Kcal energy expenditure per week. • At 28 weeks' gestation, 16/22 (73%) women in the intervention group and 8/19 (42%) women in the control group met the exercise goal of greater than 900 Kcal energy expenditure per week. • At 36 weeks' gestation, 10/19 (53%) women in the intervention group and 5/16

	(31%) women in the control group met the exercise goal of greater than 900 Kcal energy expenditure per week. • Criteria used to terminate the exercise intervention during this study included: persistent second or third trimester bleeding, placenta praevia after 26 weeks' gestation, premature labour, ruptured membranes, and pre-eclampsia.Women underwent a medical and obstetric review in this study if they experienced any of the following: unevaluated maternal cardiac arrhythmia, gestational hypertension, intrauterine growth restriction, decreased fetal movement, and new maternal symptoms including dyspnoea prior to exertion, dizziness, headache, chest pain and calf pain or swelling. • ADIPS GDM diagnostic criteria (based on 2-hour 75 gram OGTT): 1. fasting: 5.5 mmol/L. 2. 2-hour: 8.0 mmol/L. 3. 1 or more results equal to or greater than the cut-off values is required for a diagnosis of GDM.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Described as: "randomisation was done by a random number allocation technique", no further details about the random number allocation technique, probably done adequately
Allocation concealment (selection bias)	Low risk	Reported as: "randomisation was done by a random number allocation technique conducted by a third party at another location outside the hospital"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on whether outcome assessors were blinded to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	• At 20 weeks' gestation: 21/25 in intervention group (2 met criteria to terminate intervention; 2 not contactable) and 19/25 in control group (3 met criteria to terminate intervention, 2 miscarriages, 1 not contactable) completed followed up. • At 28 weeks' gestation: 22/23 in intervention group (1 met criteria to terminate intervention) and 19/20 in the control group (1 met criteria to terminate intervention) completed follow-up. • At 36 weeks' gestation: 19/22 in the intervention group (2 not contactable) and 16/19 in the control group (3 not contactable) completed follow-up. • At 6 weeks postpartum: 20/22 in the intervention

		group (2 not contactable) and 16/19 in the control group (3 not contactable) completed follow-up.
Selective reporting (reporting bias)	Low risk	No obvious risk of selective reporting.
Other bias	Low risk	No obvious risk of other bias.

Hopkins 2010

Methods	Randomised controlled trial.
Participants	98 healthy nulliparous women between 20-40 years of age, with a singleton pregnancy of less than 20 weeks' gestation Exclusion criteria: alcohol consumption or tobacco use at recruitment; a personal or family history of T2DM; development of any medical condition for which participation in an exercise program was contraindicated by the American College of Obstetricians and Gynecologists (e.g. pre-eclampsia, fetal growth restriction, preterm birth) Setting: Auckland, New Zealand.
Interventions	Women in the intervention group (n = 47) • Home-based, stationary cycling, and was individually prescribed to a maximum of 5 sessions of 40-minute aerobic exercise per week. • Fortnightly supervised exercise session, maternal HR and BP were monitored and exercise prescription was updated during the session. • Regular exercise was recommended to maintain until at least 36 weeks' gestation, after this time, participants were encouraged to maintain as close to their prescribed exercise program as possible until delivery (subject to capacity). 3 exercise phases: familiarisation (20-27 week), maintenance (28-35 week), and subject to capacity (36-40 week). Weekly energy expenditures, exercise duration and exercise intensity were averaged for each phase of exercise programme. Women in the control group (n = 37) • Continue normal daily activities for the duration of their pregnancy.
Outcomes	Maternal insulin sensitivity and body composition; infant birthweight, SGA, crown-heel length, head circumference and chest circumference; neonatal BMI, ponderal index, growth related peptides and offspring body composition
Notes	• Women in the intervention group completed 75 +/- 17% of total exercise prescribed. • Mean maternal age was higher in the intervention group: mean 31 +/- 3 years (intervention group, n = 47); mean 29 +/- 4 years (control group, n = 37); (P < 0.005). • Mean maternal BMI at trial entry was 26.7 +/- 3.3 kg/m² for women in the intervention group (n = 47) and 25.5 +/- 2.9 kg/m² in the control group; reported no significant difference in maternal trial entry BMI between women who were lost to follow-up (n = 14) and those completed the trial, but no details given on baseline characteristics of those women who lost to follow-up.
Risk of bias	

Hopkins 2010 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as "all participants were randomly assigned to exercise or control groups", no further details were available
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were unlikely to be blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on whether outcome assessors were blinded to group allocation or not
Incomplete outcome data (attrition bias) All outcomes	High risk	A total of 14 (14.3%) participants (two from the intervention group and 12 from the control group) lost to follow-up during the study period • Intervention group: 2 withdrew from study due to moving out of the area and increased work commitments). • Control group: 3 with contraindications to exercise (1 with pre-eclampsia, 1 with gestational hypertension with IUGR, and 1 with preterm labour (< 30 weeks) - all gave birth before the late gestation follow-up period); 9 withdrew (2 health concerns that did not meet exclusion criteria; 2 moved out of the Auckland area, 2 increased work commitments and 1 not wanting to have the insulin sensitivity test). Another 2 participants in the control group withdrew at the allocation stage as a result of increased work commitments (did not complete baseline testing) and wanting to take part in another exercise program during pregnancy. No information reported on whether or not these 2 participants were included in the final data analysis
Selective reporting (reporting bias)	High risk	None of the prespecified primary outcomes of this review were reported in this trial
Other bias	Low risk	No obvious risk of other bias, although not clear why groups are unbalanced (37 women in the control group and 47 women in the intervention group)

Ong 2009

Methods	Randomised control trial.
Participants	12 obese women (mean BMI [SD]: 35.1 [3.5] kg/m²) with a singleton pregnancy, a normal 18-week anatomy scan and no evidence of cardiovascular disease or pre-existent diabetes No information on exclusion criteria. Setting: Crawley, Western Australia, Australia.
Interventions	Women in the intervention group (n = 6) • 10 weeks of home-based supervised exercise (stationary cycling). • 3 sessions per week, each session involved a 10 minutes warm-up followed by 1 or 2 15 minute bouts of cycling (with rest periods if necessary) at an intensity of 50-60% $HR_{max.}$ As the weeks progressed, the exercise intensity was increased to 60%-70% $HR_{max.}$ Sessions ended with a 10-minute cool-down period of easy pedaling. Women in the control group (n = 6) • Usual daily activities. All women • Regular antenatal care. • At 18 weeks' and 28 weeks' gestation, all women had 75 gram OGTT.
Outcomes	Maternal weight change, glucose tolerance, insulin sensitivity
Notes	• Women in the intervention group completed 94% of all scheduled sessions during the 10-week study period.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Described as "women were randomly allocated into either an exercise intervention group or a control group", no other information available
Allocation concealment (selection bias)	Unclear risk	No information available on allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were unlikely to be blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information available on whether outcome assessors were blinded to group allocation or not
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up or post randomisation exclusion.
Selective reporting (reporting bias)	High risk	None of the prespecified primary outcomes of this review were reported in this trial

Ong 2009 (*Continued*)

Other bias	Low risk	No obvious risk of other bias.

Stafne 2012

Methods	Randomised control trial.
Participants	855 white women aged 18 years or older with a singleton live fetus Exclusion criteria: High-risk pregnancies or diseases that could interfere with participation (or both). Women who lived too far from the hospitals to attend weekly training groups (more than 30-minute drive) Setting: Stavanger, Norway.
Interventions	Women in the intervention group (429 women randomised, 375 women completed study): • standardised exercise program including aerobic activity, strength training, and balance exercises. • 60-minute training sessions in groups of 8-15 women instructed by a physiotherapist once a week, over a period of 12 weeks (between 20 and 36 gestation weeks). • encouraged to follow a written 45-minute home exercise program at least twice per week (30 minutes of endurance training and 15 minutes of strength and balance exercises). Women in the control group (426 women randomised, 327 women completed study): • standard antenatal care and not discouraged from exercising on their own. All women: • received written recommendations on pelvic floor muscle exercises, diet, and pregnancy-related lumbo-pelvic pain.
Outcomes	Primary outcomes: prevalence of gestational diabetes and insulin resistance Secondary outcomes: maternal weight, BMI and pregnancy complications and outcomes (e.g. newborn weight, gestational age, Apgar scores)
Notes	GDM diagnosis based on WHO criteria: • Fasting plasma BGL ≥ 7.0 mmol/L • 2-hour BGL after 75 g glucose load ≥ 7.8 mmol/L • 1 or more value(s) is (are) met or exceeded

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation was by a web-based computerised procedure in blocks of 30
Allocation concealment (selection bias)	Low risk	Described as "concealed randomisation was performed at the Unit for Applied Clinical Research, Norwegian University of Technology and Science (which was outside the

		recruiting hospitals)"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were unlikely to be blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome assessors for glucose and insulin levels were blinded for group allocation; no information on whether outcome assessors for other outcomes were blinded for group allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	375/429 women in intervention group and 327/426 women in control group completed study The Intervention group: 33/429 (7.7%) women lost to follow-up during pregnancy: 5 gave birth before follow-up; 1 medical reasons, 4 illness; 1 moved; 2 work and/or family reasons; 20 gave no reason 396 women assessed at 32-36 weeks' gestational age (then 10 answered questionnaire by mail; 11 did not complete OGTT) The control group: 61/426 (14.3%) women lost to follow-up during pregnancy: 6 gave birth before follow-up;1 medical reasons, 2 illness; 4 moved; 2 work and/or family reasons; 46 gave no reason 365 women assessed at 32-36 weeks' gestational age (then 24 answered questionnaire by mail; 14 did not complete OGTT)
Selective reporting (reporting bias)	Low risk	No obvious risk of selective reporting.
Other bias	High risk	• At baseline, women in the intervention group had lower insulin resistance. • Women lost to follow-up reported performing less regular exercise before pregnancy than women completing the study; • Among those who completed the study, women in the intervention group had lower fasting insulin and insulin resistance than women in the control group.

ACOG: American College of Obstetricians and Gynecologists
ADA: Amerian Diabetes Association
ADIPS: Australasian Diabetes in Pregnancy Society
BGL: blood glucose level
BMI: body mass index
BP: blood pressure
DM: diabetes mellitus
GDM: gestational diabetes mellitus

HR: heart rate
HR_{max}: max heart rate
IOM: Institute of Medicine
IUGR: intrauterine growth restriction
LGA: large-for-gestational age
OGTT: oral glucose tolerance test
SD: standard deviation
SGA: small-for-gestational age
T2DM: type 2 diabetes mellitus

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Chen 1997	Participants were women with abnormal 1-hour 50-gram oral glucose challenge test result (> 140 mg/dL)
Clapp 1997	A literature review, but not a report for randomised controlled trial
Clapp 2002	All participants received the same exercise intervention but different dietary interventions (high glycaemic carbohydrate diet was compared with low glycaemic carbohydrate diet)
Clapp 2002a	No outcome relating to pregnancy glucose tolerance reported.
Gaston 2009	This trial aimed to assess whether maternal-fetal disease information was a good source of exercise motivation during pregnancy. No clinically relevant outcome was reported
Haakstad 2011	No outcome relating to pregnancy glucose tolerance reported.
Hui 2006	Participants in the intervention group received both exercise and dietary interventions, data for the effects of exercise intervention on pregnancy outcomes were not able to be extracted separately
Kim 2010a	Participants were women with recent diagnosis of GDM.
Luoto 2010	This trial aimed to assess the effect of diet and exercise counselling on preventing GDM. Data for the effects of exercise counselling for GDM prevention were not able to be extracted separately
Quinlivan 2007	Exercise was not a part of the study intervention.

GDM: gestational diabetes mellitus

Characteristics of ongoing studies *[ordered by study ID]*

Chasan-Taber 2009

Trial name or title	A randomised controlled trial of prenatal physical activity to prevent gestational diabetes
Methods	RCT.
Participants	364 sedentary women, with diagnosis of GDM in a prior pregnancy according to American Diabetes Association criteria
Interventions	12-week individually tailored exercise intervention.
Outcomes	GDM, serum biomarkers associated with insulin resistance, adoption and maintenance of exercise during pregnancy
Starting date	
Contact information	Lisa Chasan-Taber: LCT@schoolph.umass.edu
Notes	

Ko 2008

Trial name or title	Effect of physical activity on metabolic syndrome in pregnancy and fetal outcome
Methods	RCT.
Participants	100 pregnant women 18-45 years old receiving prenatal care at Madigan Army Medical Center
Interventions	Intervention group will exercise 3 times per week at moderate-vigorous intensity for 45 minutes per session. Control group women will continue their usual physical activity throughout pregnancy
Outcomes	Primary outcome: central adiposity. Secondary outcome: leptin levels, glucose, insulin, cholesterol, fetal adiposity and neonatal adiposity
Starting date	October 2007.
Contact information	Cynthia W Ko: United States, Washington Madigan Army Medical Center Fort Lewis, Washington, United States, 98431
Notes	

Melo 2008

Trial name or title	Exercise and pregnancy: randomised clinical trial.
Methods	
Participants	150 women aged between 10-50 years, with singleton pregnancy (gestational age < 13 weeks), fetus alive and no previous practice of physical activity
Interventions	Walking 3 times a week during 1 hours (moderate activity).
Outcomes	Maternal primary outcome: preterm labour, weight gain, pre-eclampsia, gestational diabetes. Perinatal primary outcome: birthweight, Apgar scores, body composition, admission at neonatal intensive care unit
Starting date	April 2008.
Contact information	Adriana Melo: asomelo@gmail.com Melania Amorim: melamorim@uol.com.br
Notes	

Newnham 2011

Trial name or title	Preventing gestational diabetes mellitus using a home-based supervised exercise program during pregnancy
Methods	RCT.
Participants	200 women at 12-13 weeks' gestation, with a history of gestational diabetes in a previous pregnancy
Interventions	In addition to routine, regular antenatal care, women in the intervention group will be required to participate in 3 60-minute exercise sessions each week, starting at 14 weeks' gestation, for a total of 14 weeks (i.e. to be completed by 28 weeks of gestation). All exercise sessions will be home-based and fully supervised by an experienced exercise physiologist
Outcomes	Primary outcome measures: diagnosis of gestational diabetes mellitus (after the 14 week intervention period (28 weeks' gestation))
Starting date	April 2011.
Contact information	John Newnham: JNewnham@obsgyn.uwa.edu.au Kym Guelfi: kym.guelfi@uwa.edu.au
Notes	ClinicalTrials.gov identifier: NCT01283854

Oostdam 2009

Trial name or title	The effects of an exercise program on insulin sensitivity and plasma glucose levels in pregnant women at high risk for gestational diabetes
Methods	RCT.
Participants	160 pregnant women who are at increased risk for GDM.
Interventions	Supervised exercise program on 2 days per week during the remaining duration of the pregnancy. Each session will last for 60 minutes, consist of aerobic and strength exercises
Outcomes	Primary maternal outcome: fasting plasma glucose and relative increase in insulin resistance; primary neonatal outcome: birthweight Secondary outcome measures are: maternal serum triglycerides, maternal weight gain during pregnancy, maternal physical activity level, fetal growth
Starting date	1/10/2007.
Contact information	Corresponding author: Mireille Nm van Poppel: mnm.vanpoppel@vumc.nl
Notes	

Ramirez-Velez 2009

Trial name or title	Clinical trial to assess the effect of physical exercise on endothelial function and insulin resistance in pregnant women
Methods	RCT.
Participants	64 women, gestational age between 16-20 weeks at trial entry, who have not participated in a structured exercise program, including significant amounts of walking for the past 4 months are eligible for the trial and live fetus at the routine ultrasound scan and a normal pregnancy
Interventions	Walking (10 minutes), aerobic exercise (30 minutes), stretching (10 minutes) and relaxation exercise (10 minutes). Exercise will be performed at 3 sessions per week. All sessions will be supervised by a physical therapist and a physical educator Aerobic activities will be performed at moderate intensity (60%-70% of maximal heart rate) measured by the 6-20 Borg's rating scale. Each session starts with 5 minutes of warm up, followed by 30 minutes of aerobic activity, including 5 minutes cool down. This is followed by 15 minutes of circuit strength training of the upper limbs, lower limbs, and deep abdominal stabilisation muscles. The last 5 minutes consists of stretching and relaxation exercises
Outcomes	Primary outcome: brachial artery flow-mediated dilation. Secondary outcome: high sensitivity C-Reactive Protein, nitrates, nitrites and cyclic GMP, blood lipid profile, anthropometric indicators, functional capacity, maternal and neonatal outcomes
Starting date	October 2008.
Contact information	

Notes	

Shen 2008

Trial name or title	Impact of diet and exercise activity on pregnancy outcomes (IDEA)
Methods	RCT.
Participants	1600 healthy pregnant women with < 20 weeks' gestation.
Interventions	Aerobic exercise or walk for 3-5 times/day for 30-45 minutes/time from 20 weeks to 36 weeks of pregnancy. Dietary education on nutrition for healthy pregnancy through weekly class during pregnancy
Outcomes	Primary outcome: excessive weight gain during pregnancy. Secondary outcome: macrosomia, requirement of delivery procedures
Starting date	July 2006.
Contact information	Garry Shen: gshen@ms.umanitoba.ca
Notes	

cyclic GMP: cyclic guanosine monophosphate
GDM: gestational diabetes mellitus
RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1. Any exercise intervention versus routine care

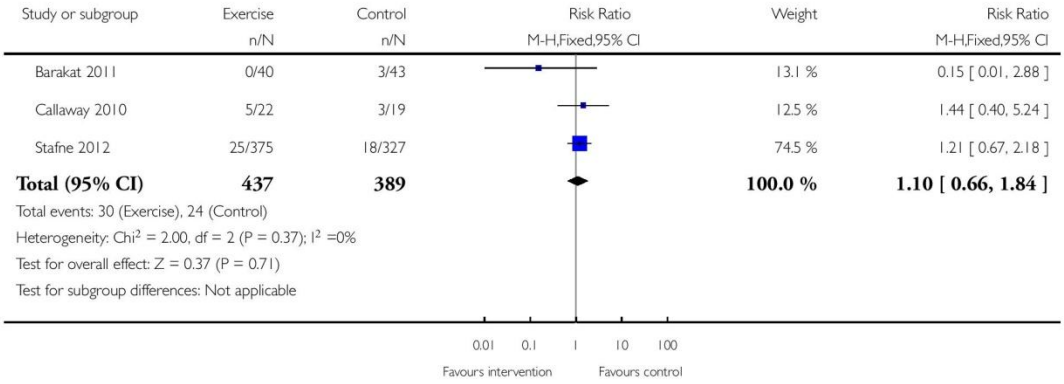
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Gestational diabetes mellitus	3	826	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.66, 1.84]
2 Caesarean section	2	934	Risk Ratio (M-H, Fixed, 95% CI)	1.33 [0.97, 1.84]
3 Operative vaginal birth	2	934	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.58, 1.17]
4 Pregnancy hyperglycaemia not meeting GDM diagnostic criteria	1	83	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.16, 7.27]
5 Weight change during pregnancy (kg)	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1 Maternal weight at late pregnancy (third trimester) (kg)	1	84	Mean Difference (IV, Fixed, 95% CI)	-1.10 [-6.11, 3.91]
5.2 Weight gain during intervention period (intervention for < one trimester)	1	12	Mean Difference (IV, Fixed, 95% CI)	-1.5 [-4.41, 1.41]
5.3 Weight gain during intervention period (intervention for > one trimester)	1	83	Mean Difference (IV, Fixed, 95% CI)	-1.30 [-2.66, 0.06]
6 Maternal BMI at late pregnancy (third trimester) (kg/m^2)	1	84	Mean Difference (IV, Fixed, 95% CI)	0.10 [-1.39, 1.59]
7 Pre-eclampsia	1	852	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.51, 1.97]
8 Birthweight	2	167	Mean Difference (IV, Fixed, 95% CI)	-102.87 [-235.34, 29.60]
9 Macrosomia (birthweight > 4000 gram)	2	934	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.68, 1.22]
10 Small-for-gestational age	1	84	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.25, 4.40]
11 Gestational age at birth (week)	2	167	Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.37, 0.29]
12 Ponderal index (gram x 100/m^3)	1	84	Mean Difference (IV, Fixed, 95% CI)	-0.08 [-0.18, 0.02]
13 Apgar score less than seven at five minutes	2	919	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.27, 3.65]
14 Admission to neonatal ward	1	838	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.39, 1.53]

Analysis 1.1. Comparison 1 Any exercise intervention versus routine care, Outcome 1 Gestational diabetes mellitus.

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 1 Gestational diabetes mellitus

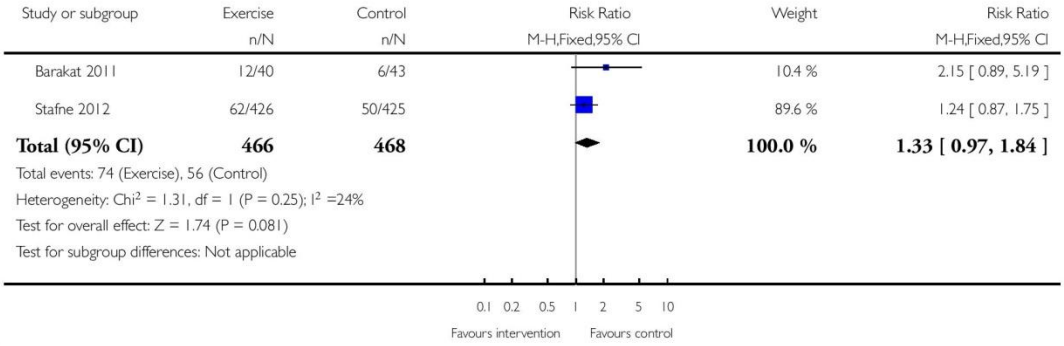


Analysis 1.2. Comparison 1 Any exercise intervention versus routine care, Outcome 2 Caesarean section.

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 2 Caesarean section

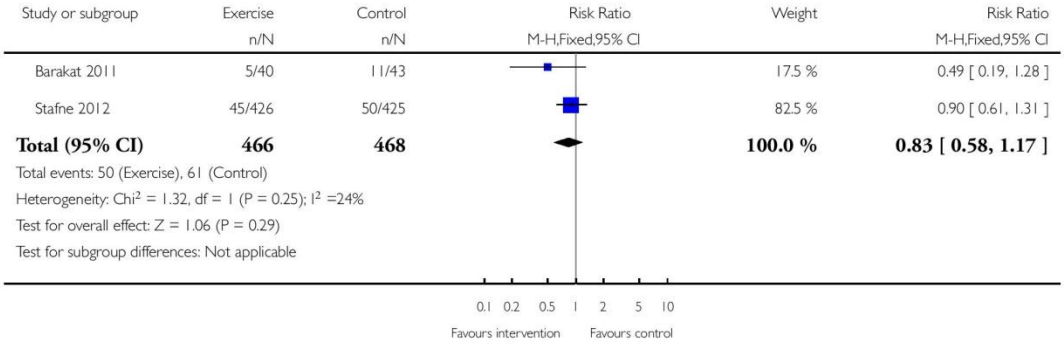


Analysis 1.3. Comparison 1 Any exercise intervention versus routine care, Outcome 3 Operative vaginal birth.

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 3 Operative vaginal birth

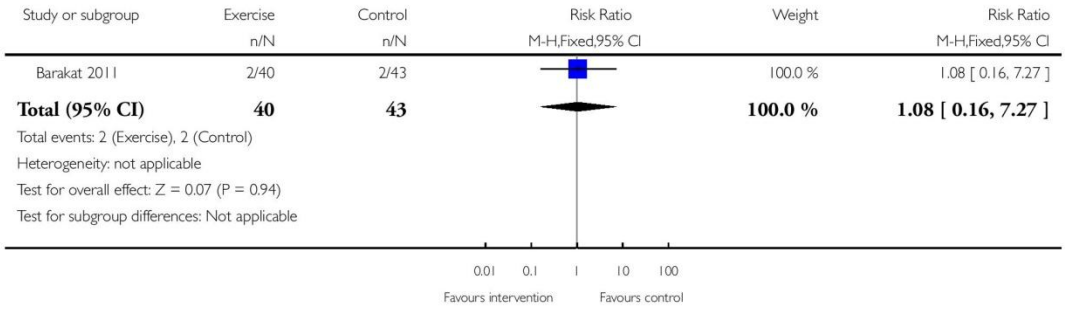


Analysis 1.4. Comparison 1 Any exercise intervention versus routine care, Outcome 4 Pregnancy hyperglycaemia not meeting GDM diagnostic criteria.

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 4 Pregnancy hyperglycaemia not meeting GDM diagnostic criteria

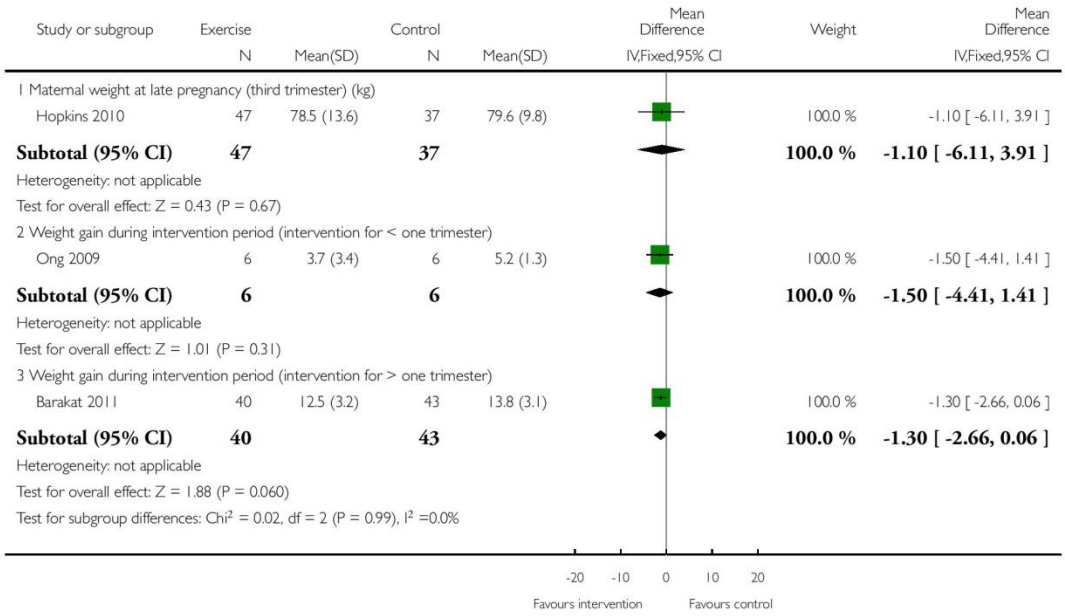


Analysis 1.5. Comparison 1 Any exercise intervention versus routine care, Outcome 5 Weight change during pregnancy (kg).

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 5 Weight change during pregnancy (kg)



Analysis 1.6. Comparison 1 Any exercise intervention versus routine care, Outcome 6 Maternal BMI at late pregnancy (third trimester) (kg/m^2).

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 6 Maternal BMI at late pregnancy (third trimester) (kg/m^2)

Study or subgroup	Exercise N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hopkins 2010	47	28.4 (4.3)	37	28.3 (2.6)		100.0 %	0.10 [-1.39, 1.59]
Total (95% CI)	**47**		**37**			**100.0 %**	**0.10 [-1.39, 1.59]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.13 (P = 0.90)

Test for subgroup differences: Not applicable

Analysis 1.7. Comparison 1 Any exercise intervention versus routine care, Outcome 7 Pre-eclampsia.

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 7 Pre-eclampsia

Study or subgroup	Exercise n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Stafne 2012	16/426	16/426		100.0 %	1.00 [0.51, 1.97]
Total (95% CI)	**426**	**426**		**100.0 %**	**1.00 [0.51, 1.97]**

Total events: 16 (Exercise), 16 (Control)

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P = 1.0)

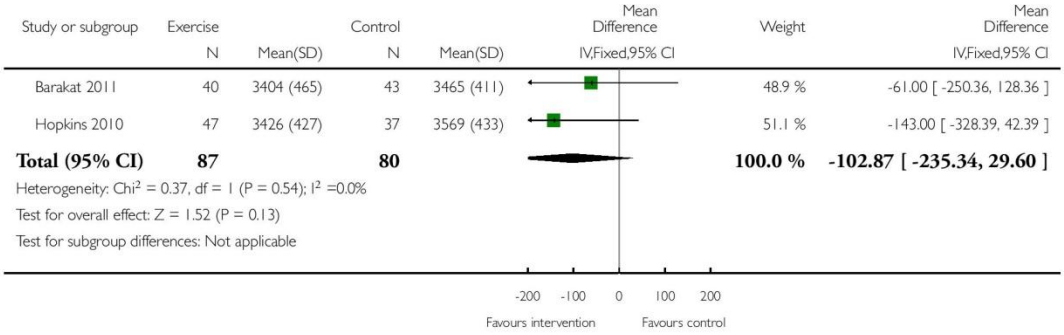
Test for subgroup differences: Not applicable

Analysis 1.8. Comparison 1 Any exercise intervention versus routine care, Outcome 8 Birthweight.

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 8 Birthweight

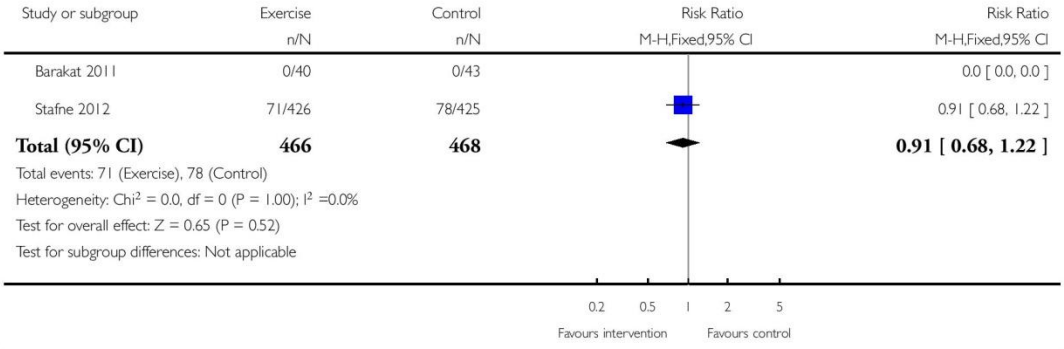


Analysis 1.9. Comparison 1 Any exercise intervention versus routine care, Outcome 9 Macrosomia (birthweight > 4000 gram).

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 9 Macrosomia (birthweight > 4000 gram)

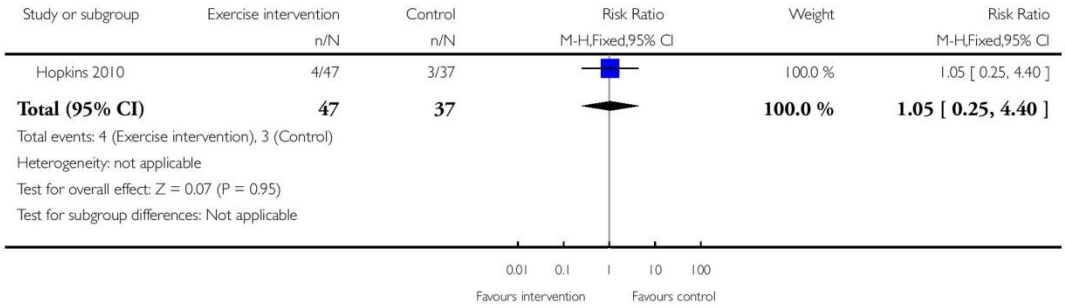


Analysis 1.10. Comparison 1 Any exercise intervention versus routine care, Outcome 10 Small-for-gestational age.

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 10 Small-for-gestational age

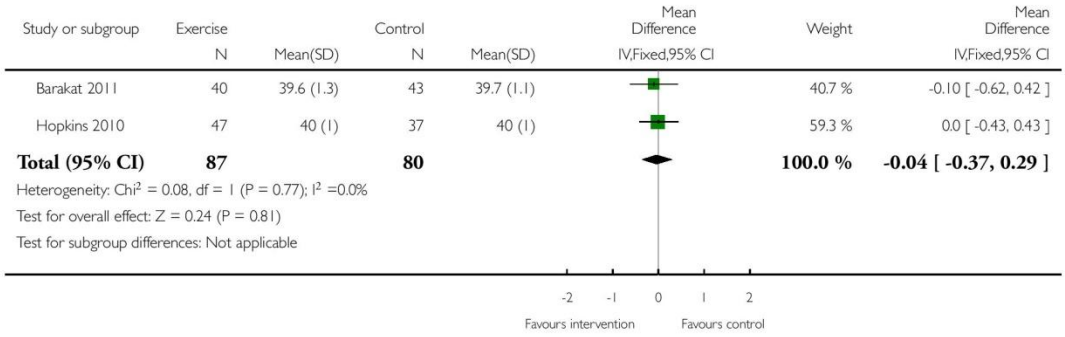


Analysis 1.11. Comparison 1 Any exercise intervention versus routine care, Outcome 11 Gestational age at birth (week).

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 11 Gestational age at birth (week)

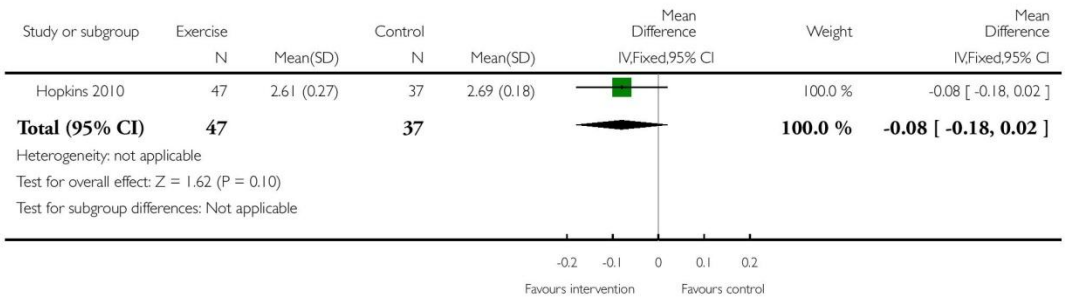


Analysis 1.12. Comparison 1 Any exercise intervention versus routine care, Outcome 12 Ponderal index (gram x 100/m^3).

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 12 Ponderal index (gram x 100/m^3)

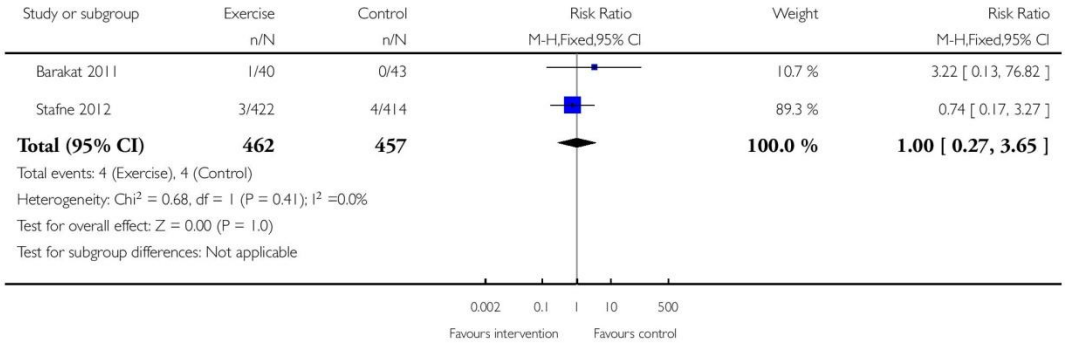


Analysis 1.13. Comparison 1 Any exercise intervention versus routine care, Outcome 13 Apgar score less than seven at five minutes.

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 13 Apgar score less than seven at five minutes

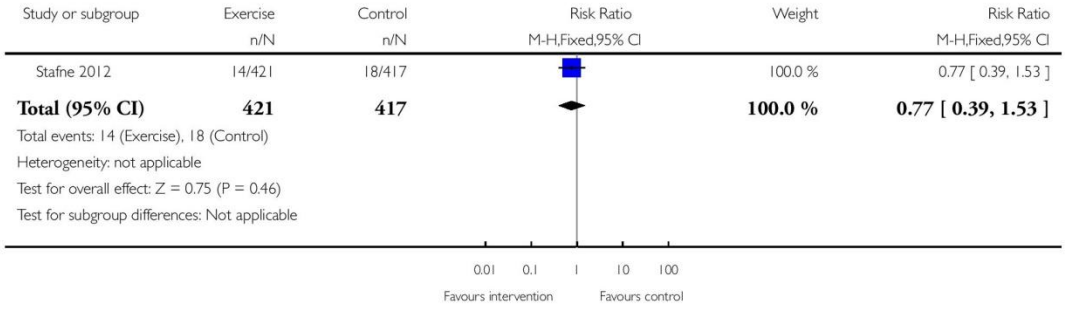


Analysis 1.14. Comparison 1 Any exercise intervention versus routine care, Outcome 14 Admission to neonatal ward.

Review: Exercise for pregnant women for preventing gestational diabetes mellitus

Comparison: 1 Any exercise intervention versus routine care

Outcome: 14 Admission to neonatal ward



APPENDICES

Appendix 1. WOMBAT Perinatal Trials Registry and ClinicalTrials.gov search strategy

We searched trials in the Women and Babies Health and Wellbeing: Action through Trials (WOMBAT) Perinatal Trials Registry using the terms of "gestational diabetes mellitus", "pregnancy", "pregnant", "glucose intolerance", "exercise", "lifestyle", "behavioural intervention". We reviewed all relevant trials listed under the search results.

We searched trials in the ClinicalTrials.gov trial registry using the terms of "exercise", "lifestyle", "behavioural intervention", "pregnancy", "pregnant", "glucose intolerance", "gestational diabetes mellitus". Then we categorised retrieved trials by topic. We selected the condition category of "Nutritional and Metabolic Diseases" and we reviewed trials listed under the conditions of "Diabetes Mellitus", "Diabetes, Gestational", "Glucose Intolerance", "Glucose Metabolism Disorders", "Hyperglycemia", "Metabolic Diseases", "Obesity", "Overnutrition".

HISTORY

Protocol first published: Issue 3, 2011

Review first published: Issue 7, 2012

CONTRIBUTIONS OF AUTHORS

Shanshan Han wrote drafts of the protocol and review, with Caroline Crowther and Philippa Middleton contributing to data extraction and all drafts.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Australian Research Centre for Health of Women and Babies (ARCH), Robinson Institute, The University of Adelaide, Australia.

External sources

- Australian Department of Health and Ageing and NHMRC, Australia.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In order to avoid duplicate information from another Cochrane review by Kramer 2006, we decided to only include studies that reported relevant outcomes on gestational diabetes mellitus, pregnancy glucose tolerance, insulin sensitivity or insulin resistance during pregnancy.

Outcome measure of 'maternal BMI at late pregnancy' was added in the review.

Weight gain during pregnancy was divided into subgroups of 'weight gain during intervention period' and 'maternal weight at late pregnancy (third trimester).

INDEX TERMS

Medical Subject Headings (MeSH)

Birth Weight; Cesarean Section [utilization]; Diabetes, Gestational [epidemiology; *prevention & control]; Exercise [*physiology]; Hyperglycemia [epidemiology]; Incidence; Infant, Newborn; Insulin Resistance [*physiology]; Pre-Eclampsia [epidemiology]; Prenatal Care; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Pregnancy

3 Cochrane systematic review: Different types of dietary advice for women with gestational diabetes mellitus

This chapter includes a published Cochrane systematic review entitled “Different types of dietary advice for women with gestational diabetes mellitus”. An authorship statement including publication details has been attached on the next page.

3.1
Statement of Authorship

Title of Paper	Different types of dietary advice for women with gestational diabetes mellitus
Publication Status	◉ Published, ○ Accepted for Publication, ○ Submitted for Publication, ○ Publication style
Publication Details	Han S, Crowther CA,Middleton P,Heatley E.Different types of dietary advice for women with gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No.: CD009275. DOI: 10.1002/14651858.CD009275.pub2.

Author Contributions

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

Name of Principal Author (Candidate)	Shanshan Han		
Contribution to the Paper	Performed data extraction and assessment of risk of bias of the included studies; performed data analysis and data interpretation; wrote drafts of the protocol and review; acted as corresponding author.		
Signature		Date	31/3/14

Name of Co-Author	Caroline Crowther		
Contribution to the Paper	Contributed to data extraction, assessment of risk of bias of the included studies, data analysis and data interpretation; commented on and edited all drafts; supervised development and the progress of work.		
Signature		Date	19/3/14

Name of Co-Author	Philippa Middleton		
Contribution to the Paper	Contributed to data extraction, assessment of risk of bias of the included studies, data analysis and data interpretation; commented on and edited all drafts; supervised development and the progress of work.		
Signature		Date	20/3/14

Name of Co-Author	Emer Heatley		
Contribution to the Paper	Performed data extraction and assessment of risk of bias of the included studies.		
Signature		Date	31/3/14

Different types of dietary advice for women with gestational diabetes mellitus (Review)

Han S, Crowther CA, Middleton P, Heatley E

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2013, Issue 3

http://www.thecochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Different types of dietary advice for women with gestational diabetes mellitus

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ABSTRACT

Background

Gestational diabetes mellitus (GDM) affects a significant number of women each year and is associated with a wide range of adverse outcomes for women and their babies. Dietary counselling is the main strategy in managing GDM, but it remains unclear which dietary therapy is best.

Objectives

To assess the effects of different types of dietary advice for women with GDM on pregnancy outcomes.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (17 May 2012) and the WOMBAT Perinatal Trials Registry (17 April 2012).

Selection criteria

Randomised controlled trials (RCTs) and cluster-RCTs assessing the effects of different types of dietary advice for women with GDM on pregnancy outcomes.

We intended to compare two or more forms of the same type of dietary advice against each other, i.e. standard dietary advice compared with individualised dietary advice, individual dietary education sessions compared with group dietary education sessions. We intended to compare different intensities of dietary intervention with each other, i.e. single dietary counselling session compared with multiple dietary counselling sessions.

Data collection and analysis

Two review authors independently assessed study eligibility, extracted data and assessed risk of bias of included studies. Data were checked for accuracy.

Main results

We included nine trials; 429 women (436 babies) provided outcome data. All nine included trials had small sample sizes with variation in levels of risk of bias. A total of 11 different types of dietary advice were assessed under six different comparisons, including:

low-moderate glycaemic index (GI) food versus high-moderate GI food,

low-GI diet versus high-fibre moderate-GI diet,

energy-restricted diet versus no energy restriction diet,

low-carbohydrate diet (≤ 45% daily total energy intake from carbohydrate) versus high-carbohydrate diet (≥ 50% daily total energy intake from carbohydrate),

high-monounsaturated fat diet (at least 20% total energy from monounsaturated fat) versus high-carbohydrate diet (at least 50% total energy from carbohydrate),

standard-fibre diet (American Diabetes Association (ADA) diet) (20 grams fibre/day) versus fibre-enriched diet (80 grams fibre/day).

In the low-moderate GI food versus moderate-high GI food comparison, no significant differences were seen for macrosomia or large-for-gestational age (LGA), (two trials, 89 babies) (risk ratio (RR) 0.45, 95% confidence interval (CI) 0.10 to 2.08), (RR 0.95, 95% CI 0.27 to 3.36), respectively; or caesarean section (RR 0.66, 95% CI 0.29 to 1.47, one trial, 63 women).

In the low-GI diet versus high-fibre moderate-GI diet comparison, no significant differences were seen for macrosomia or LGA (one trial, 92 babies) (RR 0.32, 95% CI 0.03 to 2.96), (RR 2.87, 95% CI 0.61 to 13.50), respectively; or caesarean section (RR 1.80, 95% CI 0.66 to 4.94, one trial, 88 women).

In the energy-restricted versus unrestricted diet comparison, no significant differences were seen for macrosomia (RR 1.56, 95% CI 0.61 to 3.94, one trial, 122 babies); LGA (RR 1.17, 95% CI 0.65 to 2.12, one trial, 123 babies); or caesarean section (RR 1.18, 95% CI 0.74 to 1.89, one trial, 121 women).

In the low- versus high-carbohydrate diet comparison, none of the 30 babies in a single trial were macrosomic; and no significant differences in caesarean section rates were seen (RR 1.40, 95% CI 0.57 to 3.43, one trial, 30 women).

In the high-monounsaturated fat versus high-carbohydrate diet comparison, neither macrosomia or LGA (one trial 27 babies) (RR 0.65, 95% CI 0.91 to 2.18), (RR 0.54 95% CI 0.21 to 1.37), respectively showed significant differences. Women having a high-monounsaturated fat diet had a significantly higher body mass index (BMI) at birth (mean difference (MD) 3.90 kg/m², 95% CI 2.41 to 5.39, one trial, 27 women) and at six to nine months postpartum (MD 4.10 kg/m², 95% CI 2.34 to 5.86, one trial, 27 women) when compared with those having a high-carbohydrate diet. However, these findings were based on a single, small RCT with baseline imbalance in maternal BMI.

Perinatal mortality was reported in only trial which recorded no fetal deaths in either the energy- restricted or unrestricted diet group.

A single trial comparing ADA diet (20 grams gram fibre/day) with fibre-enriched fibre enriched diet (80 grams gram fibre/day) did not report any of our prespecified primary outcomes.

Very limited data were reported on the prespecified outcomes for each of the six comparisons. Only one trial reported on early postnatal outcomes. No trial reported long-term health outcomes for women and their babies. No data were reported on health service cost or women's quality of life.

Authors' conclusions

Data for most comparisons were only available from single studies and they are too small for reliable conclusions about which types of dietary advice are the most suitable for women with GDM. Based on the current available evidence, we did not find any significant benefits of the diets investigated.

Further larger trials with sufficient power to assess the effects of different diets for women with GDM on maternal and infant health outcomes are needed. Outcomes such as longer-term health outcomes for women and their babies, women's quality of life and health service cost should be included.

PLAIN LANGUAGE SUMMARY

Different types of dietary advice for women with gestational diabetes mellitus

Each year, a significant number of pregnant women around the world develop gestational diabetes mellitus (GDM), defined as glucose intolerance or high blood glucose concentration (hyperglycaemia) that starts or is first recognised during pregnancy. Women with GDM are at risk of having instrumental birth and their babies are more likely to be large for gestational age, have a birthweight of at least 4000 grams and experience birth trauma. Although it is widely accepted that dietary counselling is the main strategy for managing women with GDM, it is not clear which dietary therapy is best. The aim of this review was to assess the effects of different types of dietary advice for women with GDM looking at pregnancy outcomes. A total of nine small randomised trials involving 437 women (444 babies), with outcome data available for 429 women and 436 babies were included in this review. Eleven different types of dietary advice were assessed within six different comparisons, including low- or moderate- glycaemic index (GI) diet compared with high- or mixed-GI diet, low-GI diet compared with high-fibre, moderate-GI diet, energy-restricted diet compared with no energy restriction diet, low-carbohydrate diet compared with high-carbohydrate diet, high-monounsaturated fat diet compared with high-carbohydrate diet, and the standard American Diabetes Association diet providing 20 grams fibre per day compared with fibre-enriched diet providing 80 grams fibre per day. Based on the current available data, we did not find that any one type of dietary advice was more effective than others in reducing the number of births that required instrumental delivery or the number of babies who were large for gestational age or had a birthweight of 4000 grams or more. The included trials had various levels of risk of bias and it remains unclear which diet is the most suitable diet for women with GDM for improving the health of women and their babies in the short and longer term. Larger, well-designed randomised trials are needed.

BACKGROUND

Description of the condition

Introduction and definition of gestational diabetes mellitus

Although there is no universally accepted diagnostic criteria (Coustan 2010), gestational diabetes mellitus (GDM) can be defined as 'glucose intolerance or hyperglycaemia (high blood glucose concentration) with onset or first recognition during pregnancy' (ACOG 2001; Hoffman 1998; Metzger 1998; NICE 2008). It is one of the most common pregnancy complications, with about 1% to 14% of pregnancies affected every year around the world (Mulla 2010). The prevalence of GDM continues to increase in line with the increasing prevalence of maternal obesity and type 2 diabetes mellitus (T2DM) (Bottalico 2007; Dabelea 2005; Mulla 2010).

Pathophysiology of gestational diabetes mellitus

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

Risk factors for gestational diabetes mellitus

A range of factors have been found to increase the risk of developing GDM (Morisset 2010). Advancing maternal age and 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) are the two most common risk factors (Morisset 2010). It is important to note that the prevalence of overweight or obesity is increasing worldwide, which is associated with increasing prevalence of GDM (Petry 2010).

High parity, non-white race/ethnicity, family history of diabetes mellitus, maternal high or low birthweight and polycystic ovarian syndrome are the known non-modifiable risk factors for GDM (Cypryk 2008; Petry 2010; Solomon 1997). The modifiable risk factors include history of having a macrosomic (birthweight 4000 grams or more) infant and history of GDM (Petry 2010). Other modifiable risk factors are lifestyle related, which include 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 overweight or obese (Hedderson 2010).

Health risks for gestational diabetes mellitus

Negative impacts of GDM on the health of women and their babies have been consistently reported (Crowther 2005; Landon 2009; Metzger 2008; Reece 2009).

Short-term risks for women with GDM include developing pre-eclampsia and increased need for induction of labour (Anderberg 2010; Crowther 2005; Dodd 2007; Ju 2008; Landon 2009; Metzger 2008) and caesarean section (Dodd 2007; Landon 2009; Metzger 2008). The incidence of cephalopelvic disproportion, uterine rupture, shoulder dystocia and perineal lacerations is increased in women with GDM due to the increased likelihood of having a large-for-gestational age (LGA) or macrosomic baby (Jastrow 2010). In the longer term, women who have a history of GDM have at least a seven-fold risk of developing T2DM in the future when compared with women who have had a normoglycaemic pregnancy (Bellamy 2009), and up to 50% of women with GDM will develop T2DM within 10 years of the index pregnancy (Kim 2002).

One of the most significant health risks for babies born to mothers with GDM is being LGA or macrosomic (Crowther 2005; Landon 2009; Metzger 2008; Reece 2009). Being a LGA fetus or macrosomic infant is a surrogate for many of the complications associated with GDM (Esakoff 2009). LGA or macrosomic infants are at increased risk of birth injury, such as shoulder dystocia, perinatal asphyxia, bone fractures and nerve palsies (Henriksen 2008; Langer 2005; Metzger 2008). Babies LGA at birth are more likely to be heavier at every age (adjusted for height) and to develop early overweight or obesity and T2DM (Pettitt 1993; Whincup 2008). In addition, babies born LGA are at increased risk of developing metabolic syndrome (a cluster of risk factors defined by the occurrence of three of the following: obesity, hypertension, hypertriglyceridaemia and low HDL cholesterol concentration) in childhood, adolescence or adulthood (Baker 1994; Guerrero-Romero 2010; Harder 2009). Development of the metabolic syndrome during childhood predicts adult T2DM at 25 to 30 years of age (Morrison 2008). These health problems repeat across generations (Mulla 2010; Petitt 1985).

Besides the risks relating to LGA or macrosomia, other perinatal risk factors for babies born to women with GDM include respiratory distress syndrome, hypoglycaemia, hyperbilirubinaemia (increased levels of bilirubin in the blood), cardiomyopathy (the deterioration of the function of the heart muscle layer), hypocalcaemia, hypomagnesaemia, polycythaemia (increase in the number of circulating red blood cells, hyperviscosity and admission to the neonatal nursery (Metzger 2008; Reece 2009; Soler 1978). Other longer-term risks for these babies include developing type 1 diabetes mellitus (Harder 2009) and having impaired neurobehavioural development (Rizzo 1997).

Management of gestational diabetes mellitus

The primary aims of management for GDM are to optimise glycaemic control and improve pregnancy outcomes (Alwan 2009; Kim 2010a). Providing dietary and lifestyle advice is usually recommended as the primary therapeutic strategy for women with GDM (ACOG 2001; Hoffman 1998; NICE 2008). If diet and lifestyle management alone are not enough to achieve good maternal glycaemic control, insulin therapy or oral hypoglycaemics such as glyburide and metformin may be indicated (ACOG 2001; Hoffman 1998; NICE 2008; Silva 2010; Simmons 2004). As a part of GDM management, maternal glucose monitoring and ultrasonography are advised to monitor treatment and to guide care for birth (ACOG 2001; Hoffman 1998; NICE 2008).

Description of the intervention

Dietary advice for managing gestational diabetes mellitus

Although it is widely accepted that diet therapy is the primary strategy for managing GDM, there is very little evidence on specific nutritional approaches such as total energy intake and nutrient distribution in GDM management (Cheung 2009; Kim 2010a; Metzger 2007). Elevated blood glucose concentrations, especially postprandial glucose elevations are associated with adverse pregnancy outcomes in GDM (De Veciana 1995). Dietary advice provided for women with GDM should ensure adequate nutrients for normal fetal growth and maternal health, but not induce weight loss or excessive weight gain during pregnancy; it also aims to assist optimal glycaemic control (ACOG 2001; Hoffman 1998; Metzger 2007; NICE 2008).

Total energy intake and weight gain during pregnancy

Given the high prevalence of overweight and obesity in women with GDM, dietary advice for appropriate pregnancy weight gain is always included as a part of nutritional management of GDM (Kim 2010a). It is estimated that the prevalence of GDM for women with a BMI within the range of 35 kg/m² to 64.9 kg/m² (extremely obese) is 15.4%, and decreases to 5.5%, 4.8% and 2.3% for women having a BMI within the ranges of 30 kg/m² to 34.9 kg/m² (obese), 25 kg/m² to 29.9 kg/m² (overweight) and 18.5 kg/m² to 24.9 kg/m² (normal weight), respectively (Kim 2010b). Small reductions in weight improve glycaemic control (ACOG 2005). However, severe calorie restriction and pregnancy weight loss are discouraged due to the risks of ketonaemia and small-for-gestational-age (SGA) infants (ACOG 2001; Hoffman 1998; NICE 2008).

In 2009, the Institute of Medicine released its new guidelines for weight gain during pregnancy, which are stratified by pre-pregnancy BMI, i.e. women with a pre-pregnancy BMI between 25 and 29.9 kg/m² should aim for 6.8 to 11.4 kg weight gain and

those with pre-pregnancy BMI of 30 kg/m² or more should aim for 5 to 9 kg weight gain (IOM 2009). However, the degree of energy restriction for pre-pregnancy overweight and obese women to achieve these weight gain goals is unknown (Kim 2010a).

The optional proportion of the total energy derived from each of the macronutrients in GDM management is still controversial (Kim 2010a). In Australia, the principles of dietary management of diabetes are also recommended for GDM management (i.e. carbohydrate contributes up to 50% total energy intake, fat accounts for less than 30% total energy and protein accounts for 10% to 20% total energy intake) (Colagiuri 2009; Hoffman 1998).

Carbohydrate and glycaemic index (GI)

Carbohydrate is an important source of energy, vitamins, minerals and fibre and is the main nutrient that affects blood glucose values (Reader 2007). Its impact on blood glucose concentrations can be affected by the total amount and type of carbohydrate (Reader 2007).

Evidence on the proportion in carbohydrate in diet therapy for GDM management is also controversial (Kim 2010a). Both low-carbohydrate diets (i.e. carbohydrate accounts for less than 42% total energy intake) and high-carbohydrate diets (i.e. carbohydrate accounts for 55% total energy intake) have been found beneficial in improving pregnancy outcomes in non-randomised studies (Clapp 2002; Major 1998; Romon 2001). These inconsistent findings triggered the hypothesis that in addition to the total amount of carbohydrate, the type of carbohydrate may also be an important factor that affects postprandial blood glucose levels (Kim 2010a). GI is a ranking of the effects of carbohydrates on blood glucose concentrations (Jenkins 1981). Foods with a low GI (less than 55) produce a lower postprandial glucose elevation and area under the curve; foods with a high GI (more than 70) produce a rapid increase in postprandial blood glucose concentrations (Jenkins 1981). In non-pregnant people with diabetes, evidence shows that using low-GI diets helps lower HbA1C and gives better glycaemic control (Thomas 2010). During pregnancy, the concept of GI is still valid (Cheung 2009). Some evidence has suggested benefits of using low-GI diets in GDM management (Moses 2009).

Fat and other nutrients

Polyunsaturated fatty acids may be protective against impaired glucose tolerance, while saturated fatty acids can increase glucose and insulin concentrations in women with GDM (Ilic 1999). However, the specific amount and sources of fat that are beneficial for GDM management are not clear (Kim 2010a). Therefore, recommendations on the fat intake for women with GDM have not yet been promulgated (ACOG 2001; Hoffman 1998; Metzger 2007; NICE 2008).

Recommendations on the intake of other nutrients for women with GDM are usually based on the general recommendations for diabetes mellitus (Cheung 2009).

Why it is important to do this review

GDM affects a significant proportion of pregnant women each year and the prevalence is increasing worldwide (Bottalico 2007; Dabelea 2005; Mulla 2010). It is associated with a range of adverse pregnancy outcomes and these adverse health outcomes can repeat across generations (Metzger 2008; Mulla 2010). Dietary counselling is the primary therapeutic strategy in GDM management (Hoffman 1998; Metzger 2007; NICE 2008). However, there is much inconsistency and uncertainty around the best dietary therapies for women with GDM (Dornhorst 2002; Kim 2010a). This review will provide reliable evidence on the effects of different dietary advice for women with GDM for improving pregnancy outcomes. One Cochrane review has addressed the effects of different diets, including low-GI diet and high-fibre diet, in pregnancy for preventing GDM (Tieu 2008). Another Cochrane review has addressed the effects of different treatments for women with GDM (Alwan 2009). In Alwan 2009, diet and exercise advice for women with GDM was compared with pharmacological treatment, additional diet and exercise advice was compared with standard antenatal care and standard diet advice was compared with individualised diet advice for women with GDM, but they did not compare different types of dietary advice, as is done in this review.

OBJECTIVES

To assess the effects of different types of dietary advice given to women with gestational diabetes mellitus (GDM) in pregnancy outcomes.

METHODS

Criteria for considering studies for this review

Types of studies

All published randomised controlled trials (RCTs) and cluster-randomised trials assessing the effects of different dietary advice for gestational diabetes mellitus (GDM) management. We intended to include published abstracts for RCTs and cluster-randomised trials if relevant outcome data were available. We planned to exclude quasi-RCTs and cross-over trials.

We planned to include trials assessing the effects of lifestyle interventions (e.g. include both providing dietary advice and physical exercise advice) in GDM management if data for the effects of dietary advice could be extracted separately.

Types of participants

Pregnant women with GDM.

Diagnostic criteria for GDM based on oral glucose tolerance test (OGTT) results were defined variously by individual trials according to the policies of local health authorities and professional organisations.

We planned to include trials recruiting pregnant women with normal glycaemia, GDM or pre-existing diabetes mellitus if subgroup data for women with GDM could be extracted separately.

Women were eligible regardless of gestation, age, parity or plurality.

Types of interventions

We planned to include any type of dietary advice for women with GDM in the review.

We planned to compare different types of dietary advice with each other. We intended to compare two or more forms of the same type of dietary advice against each other, i.e. standard dietary advice compared with individualised dietary advice, individual dietary education sessions compared with group dietary education sessions. We intended to compare different intensities of dietary intervention with each other, i.e. single dietary counselling session compared with multiple dietary counselling sessions.

Types of outcome measures

Primary outcomes

Fetal/neonatal outcomes

1. Fetal, neonatal or perinatal mortality.
2. Large-for-gestational age (LGA) (birthweight greater than or equal to 90^{th} percentile for gestational age).
3. Macrosomia (birthweight greater than 4000 g or greater than 4500 g as defined by authors).

Maternal outcomes

1. Mode of birth (normal vaginal birth, operative vaginal birth, caesarean section).

Secondary outcomes

Fetal/neonatal outcomes

1. Neonatal hypoglycaemia requiring treatment (variously defined by authors of individual trials).
2. Gestational age at birth.
3. Preterm birth (less than 37 weeks' gestation).
4. Birthweight.
5. Small-for-gestational age (SGA).
6. Shoulder dystocia.
7. Bone fracture.
8. Nerve palsy.
9. Respiratory distress syndrome.
10. Use of assisted ventilation.
11. Hyperbilirubinaemia requiring treatment.
12. Apgar scores (less than seven at five minutes).
13. Apgar scores (less than four at five minutes).
14. Ponderal index*.
15. Skinfold thickness measurements.

* A measure of leanness of a person calculated as a relationship between mass and height (can provide valid results even for very short and very tall persons).

Childhood outcomes

1. Weight.
2. Height.
3. Body mass index (BMI).
4. Fat mass/fat-free mass.
5. Skinfold thickness measurements.
6. Blood pressure.
7. Impaired glucose tolerance (as defined by author(s)).
8. Type 1 diabetes.
9. Type 2 diabetes.
10. Insulin sensitivity (as defined by author(s)).
11. Dyslipidaemia or metabolic syndrome.
12. Childhood neurodisability.
13. Educational achievement.

Adulthood

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

Maternal outcomes

Perinatal

1. Pre-eclampsia.

2. Insulin or oral hypoglycaemic agent required for hyperglycaemia.
3. Weight gain during pregnancy (according to IOM 2009 pregnancy weight gain guidelines).
4. Induction of labour.
5. Augmentation of labour.
6. Perineal trauma.
7. Postpartum haemorrhage.
8. Postpartum infection.
9. Adherence to dietary advice.
10. Women's sense of well-being and quality of life (as defined by author(s)).
11. Women's view of dietary intervention.

Long term

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

Health services cost

1. Number of hospital visits/antenatal visits for mother.
2. Dietitian visits.
3. Medical physician visits.
4. Costs to families in relation to the dietary advice provided.
5. Length of postnatal stay (mother).
6. Cost of maternal care.
7. Admission to neonatal nursery/neonatal intensive care unit.
8. Length of postnatal stay (baby).
9. Cost of offspring care.

Search methods for identification of studies

Electronic searches

We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (17 May 2012).
The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.
Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.
In addition, we searched the Women and Babies Health and Well-being: Action through Trials (WOMBAT) Perinatal Trials Registry (last searched 17 April 2012) using the search terms detailed in Appendix 1.
We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Two review authors independently assessed for inclusion all the potential studies we identified as a result of the search strategy. Disagreements were resolved through discussion and a third review author was consulted. We resolved disagreements through discussion and consulted a third review author as necessary.

Data extraction and management

We designed a form to extract data. For eligible studies, at least two review authors extracted the data using the agreed form. We resolved discrepancies through discussion. We entered data into Review Manager software (RevMan 2011) and checked for accuracy.
When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias for each 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 assessor.

(1) Sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.
We 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 each included study the method used to conceal the allocation sequence and determine whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.
We 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 each 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 were 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 each included study the methods used, if any, 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 through withdrawals, dropouts, protocol deviations)

We described for each 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, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we re-included 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 bias (checking for reporting bias)

We described for each 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 was clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review had been reported);
- high risk of bias (where not all the study's pre-specified outcomes had been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest were reported incompletely and so could not 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 sources of bias

We described for each included study any important concerns we had about other possible sources of bias.
We assessed whether each 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.

(7) Overall risk of bias

We made explicit judgements about whether studies were 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 we considered it was likely to impact on the findings. We planned

to explore the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as risk ratio with 95% confidence intervals.

Continuous data

For continuous data, we used the mean difference and 95% confidence intervals if outcomes were measured in the same way between trials. We used the standardised mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials

We did not identify any cluster-randomised trials for inclusion. However, if we identify cluster-randomised trial in future updates of this review, we will include them in the analyses along with individually-randomised trials. We will adjust their sample sizes using the methods described in the *Handbook* using an estimate of the intracluster 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. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely.
We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Dealing with missing data

For included studies, we noted levels of attrition. If we had identified studies with high levels of missing data, we would have used sensitivity analysis to explored the impact of including studies with high levels of missing data in the overall assessment of treatment effect.

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 was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the T^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if the I^2 was greater than 30% and either the T^2 was greater than zero, or there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

In future updates of this review, 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 we detect asymmetry, we will perform exploratory analyses to investigate it.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2011). We used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar. If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, we planned to use random-effects meta-analysis to produce an overall summary if an average treatment effect across trials was considered clinically meaningful. The random-effects summary would have been treated as the average range of possible treatment effects and we would have discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we did not combine trials.
When we used random-effects analyses, we have presented the results as the average treatment effect with its 95% confidence interval, and the estimates of T^2 and I^2.

Subgroup analysis and investigation of heterogeneity

If we had identified substantial heterogeneity, we would have investigated it using subgroup analyses and sensitivity analyses. We planned to consider whether an overall summary was meaningful, and if it was, use random-effects analysis to produce it.

Maternal characteristics, ways of delivering dietary advice and intensities of the dietary intervention might have significant effects on pregnancy outcomes. We planned to carry out the following subgroup analyses, however, there were insufficient data to do so.

1. Maternal characteristics

- Maternal age:
  - greater than or equal to 35 years of age will be compared with below 35 years of age.
- Ethnicity:
  - ethnic groups of Hispanic, African-American, Asian-American, native American, African, Asian and Pacific islanders and indigenous Australian compared with white ethnicity.
- Parity:
  - parity of 0 compared with 1-2;
  - parity of 0 compared with 3 or more.
- Maternal education level:
  - less than 12 years compared with 12 years or more.
- Maternal body mass index (BMI) at or before trial entry:
  - BMI ranges of 18.5 to 24.9 kg/m² compared with less than 18.5 kg/m²;
  - BMI ranges of 18.5 to 24.9 kg/m² compared with 25 to 29.9 kg/m²;
  - BMI ranges of 18.5 to 24.9 kg/m² compared with 30 kg/m² to 39.9 kg/m²;
  - BMI ranges of 18.5 to 24.9 kg/m² compared with 40 kg/m² or more.

2. Ways of delivering dietary advice

- Standard dietary advice compared with individualised dietary advice.
- Individual dietary counselling session compared with group dietary education session.
- Face-to-face dietary intervention compared with non-face-to-face dietary intervention (e.g. phone counselling, information package, etc.).

***3.* Intensities of dietary intervention**

- Single dietary counselling session compared with multiple dietary counselling sessions.

We planned to use primary outcomes in subgroup analyses.
We planned to assess differences between subgroups by interaction tests where possible.

Sensitivity analysis

We did not conduct any sensitivity analysis in this review. In future updates, we plan to carry out sensitivity analysis to explore the effects of trial quality assessed by allocation concealment and other risk of bias components, by omitting studies rated as inadequate for these components. Sensitivity analysis will be restricted to the primary outcomes.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

We identified a total of 16 trials. Fifteen trials were identified through the search conducted by the Cochrane Pregnancy and Childbirth Group and one additional trial was identified through the search of the WOMBAT (**Wom**en and **B**abies health and well-being: **A**ction through **T**rials) perinatal trial registry (WOMBAT 2011) by review authors. Following the application of eligibility criteria, we included nine trials (Balas-Nakash 2010; Cypryk 2007; Grant 2011; Lauszus 2001; Louie 2011; Magee 1990; Moses 2009; Rae 2000; Reece 1995) and excluded seven trials (Gillen 2004; Gillmer 1986; Ilic 1999; Knopp 1991; Ma 2011; Nolan 1984; Reader 2006). *See* Characteristics of included studies and Characteristics of excluded studies.

Included studies

Of the nine included trials, three were conducted in Australia (Louie 2011; Moses 2009; Rae 2000), two were conducted in the United States (Magee 1990; Reece 1995); one trial each was from Canada (Grant 2011), Denmark (Lauszus 2001), Mexico (Balas-Nakash 2010) and Poland (Cypryk 2007).

Participants

A total of 437 women and 444 babies were recruited to the nine trials, with outcome data available for 429 women and 436 babies.

Maternal trial entry weight and BMI

In Louie 2011, 68% of 92 study participants had a pre-pregnancy body mass index (BMI) of less than 25 kg/m²; the pre-pregnancy mean BMI [SD] was 23.9 [4.4] kg/m² for women in the low-GI group and 24.1 [5.7] kg/m² for those in the high-fibre moderate glycaemic index (GI) diet group. In Moses 2009, the mean trial entry BMI [SD] was 32.0 [1.2] kg/m² for the 31 women in the low-GI diet group and 32.8 [1.4] kg/m² for the 32 women in the high-GI diet group. Magee 1990 recruited 12 women who were obese at trial entry; obesity in this trial was defined as greater than 120% of their ideal body weight (according to the corrected 1959 Metropolitan Life Insurance tables) (Magee 1990). Rae 2000 included 117 women whose respective weights were greater than 110% of their ideal weight (100% ideal body weight was defined as BMI of 25 kg/m²).

Three trials did not report trial entry weight for the subgroup of women with GDM in their studies (Balas-Nakash 2010; Grant 2011; Reece 1995). Women with both GDM and T2DM were included in Balas-Nakash 2010; women with GDM and insulin-dependent diabetes were included in Reece 1995 and women with GDM and impaired glucose tolerance without meeting GDM diagnostic criteria were included in Grant 2011.

In Lauszus 2001, women were recruited after their diagnosis of GDM and were then instructed to follow a high-carbohydrate diet until the 34^{th} week of pregnancy where women were randomised into two groups. No information was reported on women's weight and BMI at recruitment, but a baseline weight was reported for women at randomisation (33 weeks of gestation) (Lauszus 2001). The mean BMI [SD] at 33 weeks' gestation were 35 [2.4] kg/m² and 32.2 [1.5] kg/m² for women in the high-monounsaturated fatty acids diet group and the high-carbohydrate diet group, respectively (Lauszus 2001),

No data were reported for women's BMI at trial entry in Cypryk 2007.

Diagnosis of GDM

Different GDM diagnostic criteria were used in the nine included trials. The Australian Diabetes in Pregnancy Society (ADIPS) criteria were used in two trials (Louie 2011; Moses 2009). One trial each used the American Diabetes Association (ADA) criteria (Magee 1990), Canadian Diabetes Association (CDA) criteria (Grant 2011) and World Health Organization (WHO) criteria (Cypryk 2007). Lauszus 2001 used three-hour 75 grams oral glucose tolerance test (OGTT) for GDM diagnosis, and GDM was defined as two or more plasma glucose samples above three standard deviations of the mean. Rae 2000 used criteria as fasting blood glucose level (BGL) greater than 5.4 mmol/L and/or two-hour BGL greater than 7.9 mmol/L in 75 grams OGTT.

There is no information on GDM diagnostic criteria in Balas-Nakash 2010 and Reece 1995.

See Characteristics of included studies for details.

Intervention and comparison

Four trials assessed the effect of a low-GI food or diet in GDM management (Balas-Nakash 2010; Grant 2011; Louie 2011; Moses 2009). In Balas-Nakash 2010, women in the low-GI diet group were advised to select low-to-moderate GI carbohydrate food, while women in the control group were allowed any type of carbohydrate food. There was no information reported on the definitions for low-GI carbohydrate, moderate-GI carbohydrate or high-GI carbohydrate in this study (Balas-Nakash 2010). Grant 2011 advised women in the low-GI diet group to select their starch food from an exchange list of low- and intermediate- GI choices, while women in the comparison group were asked to select their starch choices from an exchange list of intermediate- and high-GI food (Grant 2011). Food exchange lists for study diets were provided in the published report for Grant 2011, which indicated that the carbohydrate food recommended for women in low-GI diet group having a GI range of 26-66 and for women in the control group having a GI range of 58 to 87. In Moses 2009, women in the low-GI diet group were advised to select low-GI food (55 or less) based on the international tables of GI and glycaemic load values (Atkinson 2008) and women in the comparison group were advised to follow a high-fibre, low-sugar diet, with no specific mention of the GI.

In Louie 2011, a low-GI diet aiming for a GI target of no higher than 50, was compared with a moderate-GI diet (GI around 60).

Two trials compared an energy-restricted diet with a no energy restriction diet (Magee 1990; Rae 2000). Women in Magee 1990 were hospitalised during the intervention period. In the first week of hospitalisation, women in both groups had a 2400 kcal/day diet, with 50% total energy derived from carbohydrate, 30% from fat and 20% from protein (Magee 1990). During the second week of hospitalisation, one group of women continued the diet consumed in the first week, while women in the other group restricted their daily energy intake to 1200 kcal, which was achieved by reducing serving size without changing diet content (Magee 1990). In Rae 2000, a 6800 kJ to 7600 kJ per day diet was compared with a diet providing 8600 kJ to 9500 kJ energy.

Two trials focused on specific nutrients in the diet (Lauszus 2001; Reece 1995). Lauszus 2001 compared a high-carbohydrate diet with a high-monounsaturated fat diet, without specifying the proportion of daily energy sources for a high carbohydrate or a high monounsaturated fat. In Reece 1995, a diet containing 80 grams of fibre per day was compared with a standard ADA diet providing 20 grams fibre per day.

One trial assessed different proportions of energy derived from carbohydrate, protein and fat (Cypryk 2007). Women in the low-carbohydrate group had 45% of their daily energy from carbohydrate, 25% from protein and 30% from fat; women in the high-carbohydrate group derived 60% daily energy from carbohydrate, 25% from protein and 15% from fat (Cypryk 2007).

Therefore, we structured the comparisons as:

- Low-moderate GI food versus moderate-high GI food: Balas-Nakash 2010; Grant 2011; Moses 2009;
- Low-GI diet versus high-fibre moderate-GI: Louie 2011;
- Energy-restricted diet versus no energy restriction diet: Magee 1990; Rae 2000;
- Low-carbohydrate diet versus high-carbohydrate diet: Cypryk 2007.
- High-monounsaturated fat diet versus high-carbohydrate diet: Lauszus 2001;
- Standard-fibre (20 grams fibre/day) diet versus high-fibre (80 grams fibre/day) diet: Reece 1995.

See Characteristics of included studies for further details.

Outcome

Seven included studies focused on perinatal outcomes for women and their babies without any longer-term outcomes reported (Balas-Nakash 2010; Cypryk 2007; Grant 2011; Louie 2011; Moses 2009; Rae 2000; Reece 1995). One trial reported maternal and infant perinatal outcomes as well as maternal early postnatal outcomes of postnatal BMI and development of glucose intolerance or type 2 diabetes (up to nine months postpartum) (Lauszus 2001). One trial reported biochemical outcomes only (Magee 1990).
See Characteristics of included studies for more details.

Excluded studies

A total of six trials were excluded. We excluded three trials as they compared different types of care for women with GDM, where dietary advice was included as part of the care (Gillen 2004; Gillmer 1986; Reader 2006). Another two trials were excluded as they were cross-over studies (Ilic 1999; Nolan 1984). Knopp 1991 was excluded as it was a systematic review, not a clinical trial.
See Characteristics of excluded studies for further details.

Risk of bias in included studies

The nine included studies had various levels of risk of bias. *See* Figure 1 and Figure 2 for details.

Figure 1. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

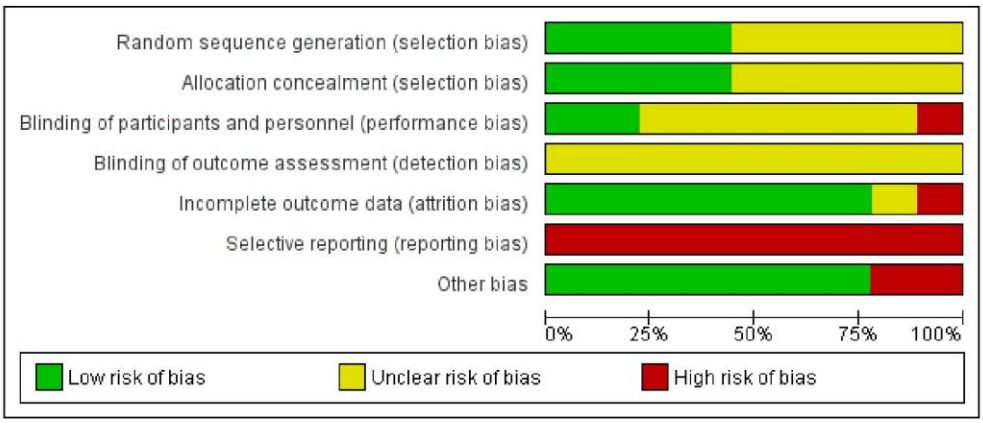
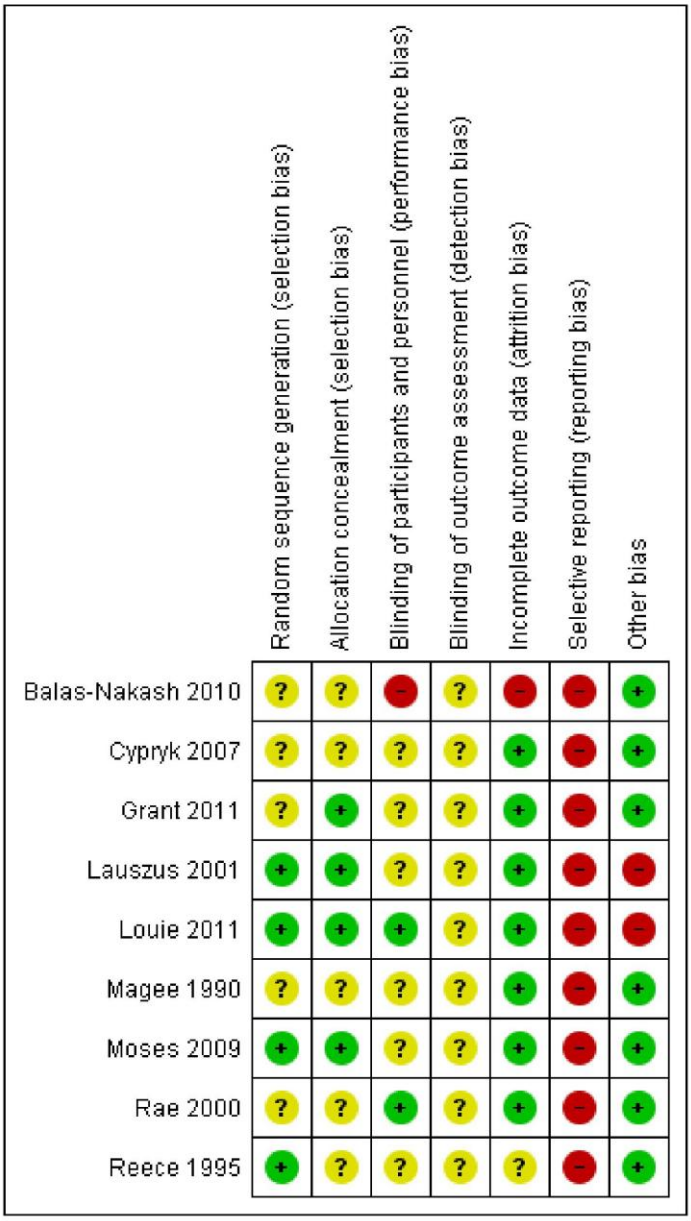


Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Four of the nine trials were at low risk of bias for sequence generation (Lauszus 2001; Louie 2011; Moses 2009; Reece 1995) with the remainder of trials unclear or not reporting this component.
Four trials reported adequate allocation concealment methods (Grant 2011; Lauszus 2001; Louie 2011; Moses 2009) with the remainder not reporting their method or not reporting it clearly.
In Grant 2011, numbered, sealed, opaque envelopes were used and the randomisation order was generated by one of the investigators who was not involved in recruitment. Randomisation in Lauszus 2001 was performed by a third person at an independent centre.
In Louie 2011, women were centrally randomised to study groups by computer-generated random numbers and the recruiter was not able to predict the allocation sequence. In Moses 2009, the allocation method was not reported in detail but was judged as likely to have been adequately concealed (women were allocated to the study groups using permuted blocks of unequal size with the list generated using STATA).

Blinding

In six trials women were not blinded (Balas-Nakash 2010; Cypryk 2007; Grant 2011; Lauszus 2001; Moses 2009; Reece 1995). Two trials reported that participants were blinded to group allocation (Louie 2011; Rae 2000). One trial did not provide information on whether or not the participants were blinded (Magee 1990).
Eight trials did not report whether the outcome assessors were blinded to group allocation (Balas-Nakash 2010; Cypryk 2007; Grant 2011; Lauszus 2001; Magee 1990; Moses 2009; Rae 2000; Reece 1995). One trial reported that the unblinded research dietitian was involved in outcome data collection (Louie 2011).

Incomplete outcome data

Seven included trials were judged as being at low risk for attrition bias (Cypryk 2007; Grant 2011; Lauszus 2001; Louie 2011; Magee 1990; Moses 2009; Rae 2000). One trial was rated as high risk of attrition bias (Balas-Nakash 2010) and another having an unclear risk of attrition bias (Reece 1995).
Three trials reported no losses to follow-up or post randomisation exclusions (Cypryk 2007; Magee 1990; Moses 2009). In Lauszus 2001, Louie 2011 and Rae 2000, small numbers of women were lost to follow up or withdrew after randomisation with reasons reported and were unlikely to affect the results. In Grant 2011, three (10.3%) women in the low-GI group withdrew after randomisation, reasons were given and data analyses were based on an intent-to-treat basis.
In Balas-Nakash 2010, of a total of 108 women potentially eligible women who were involved in another clinical trial, 20 declined (15.8%) with no reason reported and another 19 women (17.5%) were excluded due to incomplete dietary information. No information was available on the characteristics of these declined and excluded women (Balas-Nakash 2010). With the remaining 69 women in Balas-Nakash 2010, 37 were diagnosed with GDM and provided outcome data in this review. In Reece 1995, 61 women with insulin-dependent diabetes or GDM were included, 11/61 (18%) women were excluded after randomisation without specifying the numbers of women with insulin-dependent diabetes and GDM. Reasons for exclusion were reported as: spontaneous abortion (one women), moved away (two women), and noncompliant (four women in each of the study groups) (Reece 1995).

Selective reporting

All nine included trials were at high risk of reporting bias (Balas-Nakash 2010; Cypryk 2007; Grant 2011; Lauszus 2001; Louie 2011; Magee 1990; Moses 2009; Rae 2000; Reece 1995). Most of the prespecified health outcomes for women and their babies were not reported in included trials (Balas-Nakash 2010; Cypryk 2007; Grant 2011; Lauszus 2001; Louie 2011; Moses 2009; Rae 2000; Reece 1995). One trial only reported biochemical outcomes without any information provided on the health outcomes for women and their babies (Magee 1990).

Other potential sources of bias

There was no obvious risk of other potential sources of bias in seven trials (Balas-Nakash 2010; Cypryk 2007; Grant 2011; Magee 1990; Moses 2009; Rae 2000; Reece 1995).
In Lauszus 2001, women in the high-monounsaturated fat diet group had a higher trial entry BMI (mean [SD]: 35 [2.4] kg/m²) when compared with women in the high-carbohydrate group (mean [SD]: 32.2 [1.5] kg/m²). In Louie 2011, baseline blood glucose concentrations at two hours post 75 grams glucose load were significantly different between the study groups (mean [SD]: 8.6 [1.2] mmol/L for women in the low-GI group, 8.0 [1.3] mmol/L for women in the high-fibre group, P = 0.024).

Effects of interventions

Eleven different types of dietary advice for women with GDM were assessed under six different comparisons (*see* Data and analyses).

Primary outcomes

Low-moderate GI food versus moderate-high GI food

Three trials involving 126 women and their babies contributed data to this comparison (Balas-Nakash 2010; Grant 2011; Moses 2009). Authors from Grant 2011 and Moses 2009 provided additional unpublished outcome data.

Fetal or neonatal mortality was not reported in any of these trials (Balas-Nakash 2010; Grant 2011; Moses 2009). No significant differences were seen in the rates of macrosomia (two trials, 89 infants, risk ratio (RR) 0.45, 95% confidence interval (CI) 0.10 to 2.08) (Analysis 1.1) and large-for-gestational age (LGA) (two trials, 89 infants, RR 0.95, 95% CI 0.27 to 3.36) between the two study groups (Analysis 1.2). No significant differences were seen in the rates of caesarean section (one trial, 63 women, RR 0.66, 95% CI 0.29 to 1.47) (Analysis 1.3), operative vaginal birth (one trial, 63 women, RR 0.62, 95% CI 0.16 to 2.37) (Analysis 1.4) and normal vaginal birth (one trial, 63 women, RR 1.35, 95% CI 0.89 to 2.07) (Analysis 1.5) between women in the two study groups.

Low-GI diet versus high-fibre moderate-GI diet

One trial (Louie 2011) involving 92 women and their babies contributed data for this comparison. Authors were contacted for full report before the publication of this trial (Louie 2011).

No information was provided on fetal or neonatal mortality. No significant differences were seen in the rates of macrosomia (birthweight greater than 4000 g) (one trial, 92 infants, RR 0.32, 95% CI 0.03 to 2.96) (Analysis 2.1) and LGA (one trial, 92 infants, RR 2.87, 95% CI 0.61 to 13.50) (Analysis 2.2) between babies born to women in the low-GI diet group and high-fibre moderate-GI diet group. No significant difference in caesarean section rate was seen between women in the two study groups (one trial, 88 women, RR 1.80, 95% CI 0.66 to 4.94) (Analysis 2.3).

No data reported on operative vaginal birth or normal birth.

Energy-restricted diet versus no energy restriction diet

Two trials (Rae 2000 (117 women and 124 babies); Magee 1990 (12 women and their babies)) assessed the effects of energy-restricted diet for women with GDM. Magee 1990 did not report any birth outcome data.

There were no fetal deaths reported (one trial, 124 infants) (Analysis 3.1) and neonatal mortality was not reported (Rae 2000). Macrosomia was defined as birthweight at least 4000 grams or at least 90th centile weight for gender, gestational age and maternal height classified according to the Peinatal Statistics in Western Australia for macrosomia in Rae 2000. No significant differences were seen in the rates of macrosomia (one trial, 122 infants, RR 1.56, 95% CI 0.61 to 3.94) (Analysis 3.2) and LGA (one trial, 123 infants, RR 1.17, 95% CI 0.65 to 2.12) (Analysis 3.3) between babies born to women in the energy-restricted diet and no energy restriction diet.

For maternal primary outcomes, there were no significant differences seen for the rates of caesarean section (one trial, 121 infants, RR 1.18, 95% CI 0.74 to 1.89) (Analysis 3.4), operative vaginal birth (one trial, 121 infants, RR 0.98, 95% CI 0.38 to 2.54) (Analysis 3.5) and normal vaginal birth (one trial, 121 infants, RR 0.89, 95% CI 0.63 to 1.27) (Analysis 3.6) between the two study groups.

Low-carbohydrate diet ($\leq$ 45% daily total energy intake from carbohydrate) versus high-carbohydrate diet ($\geq$ 50% daily total energy intake from carbohydrate)

One trial (Cypryk 2007) involving 30 women and their babies contributed data for this comparison.

No data were reported on fetal or neonatal mortality. None of the infants were macrosomic (Analysis 4.1). There were no significant differences between the two study groups in the rates of caesarean section (one trial, 30 women, RR 1.40, 95% CI 0.57 to 3.43) (Analysis 4.2), operative vaginal birth (one trial, 30 women, RR 1.00, 95% CI 0.07 to 14.55) (Analysis 4.3) and normal vaginal birth (one trial, 30 women, RR 0.78, 95% CI 0.39 to 1.54) (Analysis 4.4).

High-monounsaturated fat diet (at least 20% total energy from monounsaturated fat) versus high-carbohydrate diet (at least 50% total energy from carbohydrate)

One trial (Lauszus 2001) involving 27 women and their babies contributed data for this comparison. The author was contacted and contributed additional unpublished outcome data.

No information was provided on fetal or neonatal mortality. No significant differences were seen in the rates of macrosomia (birthweight greater than 4000 grams) (one trial, 27 infants, RR 0.65, 95% CI 0.19 to 2.18) (Analysis 5.1) and LGA (one trial, 27 infants, RR 0.54, 95% CI 0.21 to 1.37) (Analysis 5.2) between babies born to women in the high-monounsaturated fat diet group and to women in the high-carbohydrate diet group.

No data on maternal primary outcomes was reported.

Standard-fibre (20 grams fibre/day) diet versus high-fibre (80 grams fibre/day) diet

One trial involving 22 women with GDM and their babies contributed data to this comparison (Reece 1995).

No data were available on maternal and child primary outcomes under this comparison.

Secondary outcomes

Low-moderate GI food versus moderate-high GI food

No significant differences were seen between the two study groups for the outcomes of birthweight, gestational age at birth, small-for-gestational age (SGA), induction of labour and preterm birth

(Analysis 1.6; Analysis 1.7; Analysis 1.8; Analysis 1.9; Analysis 1.10). A random-effects analysis was used for the outcome of insulin or oral hypoglycaemic agent required for hyperglycaemia as significant heterogeneity was noted ($Tau^2 = 0.41$; $I^2 = 78\%$). This may due to the different criteria used in different trials for hypoglycaemic agents (Balas-Nakash 2010; Grant 2011; Moses 2009). On average, there was no significant difference in the use of insulin or hypoglycaemic agent between women in the two study groups, but the treatment effects of two trials were strongly in opposite directions, so it is possible that both positive and negative effects will be found in different trials and populations (Analysis 1.11).

In Balas-Nakash 2010, women's adherence to dietary advice was assessed by three different methods including adaption of calorie intake, adherence questionnaire and self-perception of adherence. There were no subset data reported on the adherence to dietary advice for women with GDM (Balas-Nakash 2010). Grant 2011 reported all participants in the low-GI group rated the foods as being "good" and indicated they would consider continuing these low-GI foods postpartum; no separate data were reported on adherence to diet advice for the women with GDM. No information was reported on women's adherence to dietary advice in Moses 2009.

There were no data reported on other prespecified secondary review outcomes.

Low-GI diet versus high-fibre moderate-GI diet

There were no significant differences in birthweight (one trial, 92 infants, mean difference (MD) 0.00 g, 95% CI -277.18 to 277.18) (Analysis 2.4). Gestational age at birth (one trial, 92 infants, MD -0.10 weeks, 95% CI -0.39 to 0.19) (Analysis 2.5); preterm birth (one trial, 92 infants, RR 0.96, 95% CI 0.14 to 6.51) (Analysis 2.6) and SGA (one trial, 92 infants, RR 1.20, 95% CI 0.34 to 4.18) (Analysis 2.7) showed no differences between groups. No significant differences were seen in the ponderal index for infants born to women in the two study groups (one trial, 92 infants, MD 0.20 kg/m³, 95% CI -0.79 to 1.19) (Analysis 2.8).

Gestational weight gain for women in the low-GI diet group was not significantly different when compared with the high-fibre moderate-GI diet group (one trial, 87 women, MD -1.20 kg, 95% CI -3.43 to 1.03) (Analysis 2.9). There was no significant difference seen in the number of women required insulin treatment for hyperglycaemia between the two study groups (one trial, 92 women, RR 0.83, 95% CI 0.58 to 1.17) (Analysis 2.11). Adherence to dietary intervention was assessed by a 24-hour recall when women were attending their dietitian appointments (Louie 2011); there was no significant difference seen in the number of women who were adherent to the study diets (one trial, 92 women, RR 0.84, 95 %CI 0.64 to 1.11) (Analysis 2.10).

There were no data available on other prespecified secondary review outcomes.

Energy-restricted diet versus no energy restriction diet

There were no significant differences in the outcomes of induction of labour (one trial, 114 women, RR 1.02, 95% CI 0.68 to 1.53) (Analysis 3.7), pre-eclampsia (one trial, 117 women, RR 1.00, 95% CI 0.51 to 1.97) (Analysis 3.8) and insulin required for maternal hyperglycaemia (one trial, 117 women, RR 1.05, 95% CI 0.47 to 2.34) (Analysis 3.9). Fasting plasma glucose and fasting plasma insulin were reported in a single, small randomised trial involving 12 women; no significant differences were see in fasting plasma glucose (standardised mean difference (SMD -0.35 mmol, 95% CI -1.51 to 0.81) and fasting plasma insulin (SMD -0.17 pM, 95% CI -1.32 to 0.98) between the two study groups (Analysis 3.10). Outcomes including shoulder dystocia, birthweight, gestational age at birth were reported in one trial (Rae 2000) but since numbers in each group were unclear or these outcomes, no data were able to be included in the review.

Adherence to dietary intervention in Rae 2000 was assessed by three-day food diaries. Women in the energy-restricted diabetic diet group consumed slightly less (97%) energy than the diet goal of 6800 kJ/day to 7600 kJ/day; whereas women in the no energy restriction diabetic diet consumed considerably less energy (77%) than the dietary goal of 8600 Kj/day to 9500 Kj/day. As a result, there was no significant difference between average daily energy intake between women in the two groups (Rae 2000).

No data were reported on other secondary review outcomes.

Low-carbohydrate diet (≤ 45% daily total energy intake from carbohydrate) versus high-carbohydrate diet (at least 50% daily total energy intake from carbohydrate)

There were no significant differences seen in birthweight (one trial, 30 infants, MD 22.00 g, 95% CI -241.06 to 285.06) (Analysis 4.5) or gestational age at birth (one trial, 30 infants, MD 0.10 week, 95% CI -0.83 to 1.03) (Analysis 4.6) between the two study groups. Adherence to dietary advice was reported as 12/15 (80%) in the low-carbohydrate group and 11/15 (73.3%) in the high-carbohydrate diet group (full adherence to recommended menu) (Cypryk 2007). Twenty (66.7%) women reported no symptoms of hunger, seven women reported hunger after breakfast on the first few days of the study period and three women reported most intense hunger before breakfast (Cypryk 2007). None of the women experienced any symptoms of intolerance towards the recommended diets (Cypryk 2007).

There were no data reported on other prespecified secondary review outcomes.

High-monounsaturated fat diet (at least 20% total energy from monounsaturated fat) versus high-carbohydrate diet (at least 50% total energy from carbohydrate)

There were no significant differences in birthweight (one trial, 27 infants, MD 1.00 g, 95% CI -112.85 to 114.85) (Analysis 5.3)

and gestational age at birth (one trial, 27 infants, MD 0.10 week, 95% CI -0.13 to 0.33) (Analysis 5.4).

None of the women developed pre-eclampsia (Analysis 5.5) or needed insulin for hyperglycaemia (Analysis 5.6) (Lauszus 2001). Women in the high-monounsaturated fat diet group were significantly heavier in late pregnancy (third trimester) (Analysis 5.7) and had a significantly higher BMI during late pregnancy (third trimester) (Analysis 5.8) and at six to nine months postpartum (one trial, 27 women, MD 4.10 kg/m², 95% CI 2.34 to 5.86) (Analysis 5.9), when compared with women in the high-carbohydrate diet group. However, it is important to note a significant BMI difference existed at trial entry between women in the two study groups, and in the original analysis carried out by the authors was adjusted for BMI (Lauszus 2001). There were no significant differences seen in the incidence of developing type 2 diabetes within six weeks postpartum (one trial, 24 women, RR 2.00, 95% CI 0.45 to 8.94) (Analysis 5.10) and four months or more postpartum (one trial, six women, RR 1.00, 95% CI 0.10 to 9.61) (Analysis 5.10) between women in the two study groups. No significant differences were seen in the incidence of developing glucose intolerance without meeting type 2 diabetes diagnostic criteria within six weeks postpartum (one trial, 24 women, RR 1.50, 95% CI 0.30 to 7.43) (Analysis 5.11) and four months or more postpartum (one trial, seven women, RR 0.27, 95% CI 0.01 to 4.93) (Analysis 5.11). Insulin sensitivity was assessed by using an intravenous glucose tolerance test (Galvin 1992), with no significant difference seen in maternal fasting glucose, fasting insulin and insulin sensitivity during pregnancy between the two study groups.

There were no data available on other prespecified secondary review outcomes.

Standard-fibre (20 grams fibre/day) diet versus high-fibre (80 grams fibre/day) diet

When compared with infants born to women having a standard ADA diet (with 20 grams fibre per day), there were no significant difference seen in birthweight (one trial, 22 infants, MD -94.00 g, 95% CI -446.71 to 258.71) (Analysis 6.1) and gestational age at birth (one trial, 22 infants, MD 0.00 week, 95% CI -1.30 to 1.30) (Analysis 6.2). No women required insulin treatment for hyperglycaemia during pregnancy (Reece 1995) (Analysis 6.3). No significant difference was seen in gestational weight gain between women in the two study groups (one trial, 22 women, MD 2.40 kg, 95% CI -2.20 to 7.00) (Analysis 6.4). No information was given on the start and end point weights used for calculating weight change in the trial provided outcome data (Reece 1995).

Women were instructed to keep daily food records for assessing their compliance to the study dietary intervention (Reece 1995). Dietary compliance was rated as good in 60% and acceptable in 40% of the whole sample size, which included both women with type 2 diabetes and GDM (Reece 1995). No subset data were reported on the adherence to dietary advice for women with GDM (Reece 1995).

No data were available on other prespecified secondary review outcomes.

Subgroup analyses and sensitivity analyses

Due to the small number of studies included and limited data available, no subgroup analyses and sensitivity analyses were conducted.

DISCUSSION

Summary of main results

Diet comparisons including low-moderate GI food versus high-moderate GI food; low-GI diet versus high-fibre moderate-GI diet; energy-restricted diet versus no energy restriction diet; low-carbohydrate diet versus high-carbohydrate diet; high-monounsaturated fat diet versus high-carbohydrate diet; standard-fibre diet providing 20 grams fibre per day versus fibre-enriched diet providing 80 grams fibre per day were investigated in this review.

No significant differences were seen in any of the reported primary outcomes. Based on the current very limited data, it remains unclear which diet is the most suitable diet for women with GDM in improving the health for women and their babies in the short or long term.

Overall completeness and applicability of evidence

The evidence on different dietary advice for women with GDM is incomplete. Although a wide range of dietary advice was investigated, very limited outcome data were reported for each of the dietary comparisons and most reported outcomes were based on data from individual studies.

In the comparison of standard ADA diet (20 grams fibre/day) versus fibre-enriched diet (80 grams fibre/day), none of the review's primary outcomes were reported (Reece 1995). One trial reported biochemical outcomes only, without any information provided on clinical outcomes for the women and their babies under the comparison of energy-restricted diet versus no energy restriction diet (Magee 1990). For longer term outcomes, only very limited data from one small randomised trial were available on postpartum BMI, future development of type 2 diabetes and future development of glucose intolerance without meeting type 2 diabetes diagnostic criteria (Lauszus 2001). No data were available on any other maternal or child longer term outcomes and health service cost.

Due to the small number of studies involved in each of the dietary comparisons, various levels of risk of bias of the included studies and small numbers of participants, the applicability of the current available evidence was very limited.

Quality of the evidence

A total of nine small trials were included (437 women, 444 babies); outcome data were available from 429 women and 436 babies .

The majority of the comparisons in this review were based on data from one or two small trials. The quality of the evidence for each of the dietary comparisons greatly depends on the quality of the one or two trial(s) which provided outcome data.

Risk of bias varied across the nine included trials in this review. Four included studies (Grant 2011; Lauszus 2001; Moses 2009; Rae 2000) had low-to-moderate risk of bias. Three included trials (Cypryk 2007; Louie 2011; Reece 1995) were of moderate-to-high risk of bias. Published reports for Balas-Nakash 2010 and Magee 1990 did not allow a detailed assessment of their risk of bias. Due to the nature of behavioural interventions, blinding of participants was not implemented in six out of the nine trials (Balas-Nakash 2010; Cypryk 2007; Grant 2011; Lauszus 2001; Moses 2009; Reece 1995). Blinding of outcome assessor(s) was unclear in all nine included trials (Balas-Nakash 2010; Cypryk 2007; Grant 2011; Lauszus 2001; Louie 2011 Magee 1990; Moses 2009; Moses 2009; Rae 2000; Reece 1995).

Women's adherence to dietary interventions may have had an impact on outcomes of interventions, with some suggested dietary changes easier to adopt than others. Furthermore, in Rae 2000, there was no significant difference between average daily energy intake between women in the energy-restricted diabetic diet group and group with no energy restriction, which may have contributed to the research findings of no significant difference on pregnancy outcomes between women in the two groups. In Lauszus 2001, authors referred to study groups as high-carbohydrate diet group and high-monounsaturated fatty acids diet without giving a clear definition about this in terms of foods, making it hard to judge women's adherence. In Balas-Nakash 2010, Grant 2011 and Reece 1995, a mixed population including women with type 2 diabetes and women with GDM were included. None of the three trials reported dietary adherence for the subgroup of women with GDM; or the GI values of their actual food intake (Balas-Nakash 2010; Grant 2011; Reece 1995).

The remaining four trials did not report information about women's adherence to dietary interventions (Cypryk 2007; Louie 2011; Magee 1990; Moses 2009).

Potential biases in the review process

Systematic searches of all potential eligible trials were carried out by the Trials Search Co-ordinator of the Cochrane Pregnancy and Childbirth Group. We also searched the WOMBAT (**Wom**en and **B**abies health and wellbeing: **A**ction through **T**rials) perinatal trial database (WOMBAT 2011) (Last Search: 17 April 2012) and reference list of the identified potential trials. Authors of the included trials were also contacted via email for additional data where possible during the review process.

One potential bias introduced during the review process may be the definition of eligible women for this review. We used the definition of GDM according to the diagnostic criteria selected by trial authors. Due to the inconsistencies existing in GDM diagnostic methods around the world, we may have included women with various degrees of pregnancy hyperglycaemia.

Another possible bias may have been introduced when we grouped trials under different comparisons for data synthesis. For the comparison of low-carbohydrate diet versus high-carbohydrate diet, there was only one trial that provided outcome data (Cypryk 2007). In this trial, women in the low-carbohydrate diet group had a 30% energy from fat while those in the high-carbohydrate diet group had only 15% energy from fat (Cypryk 2007). A 50% difference in diet fat content may have introduced bias to a comparison that focused on carbohydrate only. In addition, in the comparison of energy-restricted diet versus no energy restriction diet, the two trials included under this comparison actually had different levels of energy restrictions; one trial had 50% energy restriction and the other had 20% to 30% energy restriction (Magee 1990; Rae 2000). Combining evidence from two trials with different levels of energy restriction may have introduced bias, although in this current review, only one of the two trials contributed outcome data.

Agreements and disagreements with other studies or reviews

In this review, we did not find enough evidence to suggest the most suitable diet compositions for women with GDM in improving pregnancy outcomes.

There is a systematic review assessing the effect of low-GI diet for women with GDM (Louie 2010). Only one randomised clinical trial (Moses 2009) involving 63 women, was included in this review (Louie 2010). Louie 2010 found a significantly lower proportion of women in the low-GI group met the criteria to commence insulin than women in the high-GI group and there were no significant differences in any other reported pregnancy outcomes. In our review, three included trials involving 126 women contributed data on the outcome of requirement of insulin for pregnancy hyperglycaemia. One trial was the same trial included in Louie 2010. We did not find a significant difference in the requirement of insulin for pregnancy hyperglycaemia for women in the low-GI group when compared with women in the high-GI group; we also did not find any significant differences in other primary and secondary outcomes under this comparison.

Modest calorie restriction, defined as 1600 to 1800 kcal/day or a 33% energy reduction was reviewed in two review papers (Knopp 1991; Reader 2007). Both review papers reported the benefits of optimising glycaemic control and regulating pregnancy weight gain, without increasing the risk of ketosis by having a modest calorie restriction diet for obese women with GDM (Knopp 1991; Reader 2007). Neither reviews report data on pregnancy outcomes (Knopp 1991; Reader 2007). In our review, two trials investigated the effects of energy restriction for women with GDM (Magee 1990; Rae 2000). Pregnancy outcome data were only available from one of the two trials (Rae 2000), which assessed the effects of diet with 20% to 30% energy restriction for women with GDM. We did not find any significant differences in the reported primary outcomes of fetal mortality, macrosomia, large-for-gestational age and mode of birth or the reported secondary outcomes. However, it is important to note that the actual daily energy intake for women in Rae 2000 was not significantly different between the two study groups.

AUTHORS' CONCLUSIONS

Implications for practice

Overall, results were inconclusive due to the very limited number of trials, participants and data available for each of the six dietary comparisons. Women having a high-monounsaturated fat diet (contributing at least 20% total daily energy intake) are more likely to be heavier during the third trimester and have a higher late pregnancy BMI and postnatal BMI when compared with women having a high-carbohydrate diet (contributing at least 50% total daily energy intake). However, it is important to note that these findings are based on very limited data often from single, small randomised trials with data unadjusted for trial entry imbalance in maternal BMI. In our review, we did not find any other significant benefits or harms of the diets investigated under the six comparisons.

No conclusive suggestions on the most appropriate diets for women with GDM can be made based on currently available evidence from randomised controlled trials.

Implications for research

Further larger trials with sufficient power to assess the effects of different diets for women with GDM on maternal and infant health outcomes are needed. Participants' adherence to dietary interventions and methods about improving intervention adherence need to be addressed and reported. Multi-faceted dietary interventions (i.e. a dietary intervention targeting total energy, proportion of energy from different macronutrients and glycaemic index) may be worth considering when designing future trials. Outcomes such as longer-term health outcomes for women and their babies, women's quality of life and health service cost should be included.

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As part of the pre-publication editorial process, this review has been 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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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Balas-Nakash 2010

Methods	Randomised controlled trial.
Participants	N = 37 (a total of 69 women were involved in the study, but only 37 women were diagnosed with GDM and provided outcome data for this review) Women of ≤ 30 weeks' gestation, diagnosed with Type A2 GDM (see notes), who were planning to give birth at the NIPerIER and who required medical treatment from the Department of Endocrinology at NIPerIER Exclusion criteria: women with T1DM, Type A1 GDM (see notes), glucose intolerance, multiple pregnancies, kidney or liver disease and hyper or hypothyroidism Setting: Mexico.
Interventions	Low-to-moderate GI diet group (n = 19): only foods with a low-to-moderate GI were recommended Control group (n = 18): any type of carbohydrate was permitted All women: 1. received medical nutrition therapy from a nutritionist and diabetes educator, which included a complete evaluation of nutritional status, nutritional intervention based on a moderate restriction of calorie (24 kcal/kg) and carbohydrate (40% to 45%) intake; 2. weight, weight gain, glycaemic control and initiation of or any alteration to insulin treatment were evaluated in each consultation; 3. received a glucose meter and a finger prick device; frequent capillary glucose self-monitoring (6 times a day) as an intense educational component; 4. were informed about the importance of measuring their glucose levels, how to use the glucose meter and about the recording of capillary glucose readings.
Outcomes	Adherence to dietary intervention, diet intake, weight change, insulin use
Notes	1. No GDM diagnostic criteria reported. 2. Type A1 GDM: abnormal OGTT but normal BGLs during fasting and 2 hours after meals; diet modification is sufficient to control glucose levels. 3. Type A2 GDM: abnormal OGTT compounded by abnormal glucose levels during fasting and/or after meals; additional therapy with insulin or other medications is required.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as "women included in this study were randomly divided into two study groups", no further information available
Allocation concealment (selection bias)	Unclear risk	No information was given on allocation concealment.

Balas-Nakash 2010 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	It is not feasible to blind study participants due to the nature of behavioural intervention. No information on whether research personnel were blinded or not
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information about whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	Of the total randomised cohort of 108 eligible women (mixed cohort of women with GDM and T2DM) in a clinical trial, 20 declined (15.8%) to participate in the current trial with reasons unclear. Another 19 women (17.5%) were excluded due to incomplete dietary information. No information was available for these excluded participants
Selective reporting (reporting bias)	High risk	Most of the prespecified review outcomes were not reported in this trial
Other bias	Low risk	No obvious risk of other bias.

Cypryk 2007

Methods	Randomised controlled trial.
Participants	N = 30. Caucasian women with newly diagnosed GDM according to WHO criteria (see notes) Exclusion criteria not reported. Setting: Poland.
Interventions	Low-carbohydrate diet group (n = 15): daily total energy divided as carbohydrate:45%, protein: 25%, fat: 30% (based on daily total energy of 1800 Kcal). Women were encouraged to have the diet until birth High-carbohydrate diet group (n = 15): daily total energy divided as carbohydrate: 60%, protein: 25%, fat: 15% (based on daily total energy of 1800 Kcal). Women were encouraged to have the diet until birth All women: 1. before dietary intervention, BGL were recorded from the patients' diaries 3 to 4 days before study intervention; 2. during the first 14 days after the start of interventions, women were asked to HBGM 4 times a day (fasting and 2 hours after breakfast, lunch and dinner); results were recorded in the HBGM diary; 3. on day 15, compliance to nutritional recommendations was assessed, diary reviewed; 4. urine ketones were checked daily.
Outcomes	Obstetric outcomes, BGL, intervention compliance, side-effects of the diet intervention

Cypryk 2007 (*Continued*)

Notes	GDM diagnosis based on WHO criteria: • fasting BGL ≥ 7.0 mmol/L; • 2-hour BGL after 75 g glucose load ≥ 7.8 mmol/L; • 1 or more value(s) is (are) met or exceeded.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Described as "the patients were randomised into two groups", no further details available
Allocation concealment (selection bias)	Unclear risk	No information was given on allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It was not feasible to blind study participants. No information on whether research personnel were blinded or not
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information about whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up or post randomisation exclusion.
Selective reporting (reporting bias)	High risk	Most of the prespecified review outcomes were not reported in this trial
Other bias	Low risk	No obvious risk of other bias.

Grant 2011

Methods	Randomised controlled trial.
Participants	N = 29 Pregnant women aged at 18 to 45 years, diagnosed with GDM according to CDA criteria, and who had been referred to the Diabetes in Pregnancy Clinic (DIP), St.Michael's Hospital, Canada Exclusion criteria: presence of a multiple pregnancy or an acute or chronic illness affecting carbohydrate metabolism; presence of type 1 or type 2 diabetes prior to the current pregnancy; use of insulin treatment prior to providing consent; greater than 34 weeks' gestation; and unable to communicate in English with no translator available Setting: Canada.
Interventions	Low-GI diet group (n = 13): participants were asked to select their starch choices from an exchange list of low-GI foods Intermediate or high-GI diet group (n = 16): participants were asked to select their starch choices from an exchange list of intermediate- and high-GI foods, reflecting the usual

	intake of typical DIP clinic patients All women: 1. standard Medical nutrition therapy: patients were introduced to the Diabetes Food Guide and Canadian dietary recommendations to support a healthy pregnancy. Clinic dietitian recommended how many starch choices/ servings each participant should consume at each mean based upon their own individual gestational energy requirements and Acceptable Macronutrient Distribution Ranges; 2. provision of approximately $20/week worth of non-perishable study foods and all blood testing strips; 3. self-monitored blood glucose from baseline to week 8: 4 times a day (fasting, 2-h after breakfast, lunch and dinner); 4. insulin therapy if self-monitored blood glucose were not met with lifestyle modification within 2 to 3 weeks.
Outcomes	Primary outcomes: fasting serum glucose and HbA1c at baseline and 4 weeks after intervention; SMBG from baseline to week 8 Secondary outcomes: serum glucose, insulin, lipids and C-reactive protein at baseline and 4 weeks after intervention, maternal dietary intake, physical activity (time, type and duration), birthweight, use of insulin, macrosomia (birthweight ≥ 4000 g), LGA (> 90th percentile population specific), SGA (< 10th percentile population specific)
Notes	CDA criteria used for GDM diagnosis: • fasting: 5.3 mmol/L; • 1-h 75-g OGTT: 10.6 mmol/L; • 2-h 75-g OGTT: 8.9mmol/L; • GDM: 2 of the values are met or exceeded.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomisation order was created by one of the investigators who was not involved in recruitment. It is unclear how the sequence was generated, but it is likely to be a computer-generated sequence
Allocation concealment (selection bias)	Low risk	Sealed, numbered, opaque envelopes were used, and various block sizes in randomisation were used
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Described as an "open-label" pilot study.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 women (10.3%) in the low-GI group withdrew after randomisation, reasons given. Data were analysed on an

Grant 2011 (*Continued*)

		intent-to-treat basis
Selective reporting (reporting bias)	High risk	Only limited data were reported on some of the prespecified review outcomes
Other bias	Low risk	There is no obvious risk of other bias.

Lauszus 2001

Methods	Randomised controlled trial.
Participants	N = 27. Women with a positive 3-hour 75 g OGTT before the 34 weeks' gestation Exclusion criteria: use of any hypoglycaemic, anti-lipidaemic or antihypertensive medication
Interventions	High-carbohydrate diet group (n = 14): from 34 weeks' gestation women had a high carbohydrate diet, no details about high carbohydrate diet High-monounsaturated fat diet group (n = 13): from 34 weeks' gestation women had a high-monounsaturated fat diet, no details about high-monounsaturated fat diet All women: after being diagnosed with GDM, all women were instructed to follow a high-carbohydrate diet until the 34^{th} week.
Outcomes	Pre-eclampsia, glycaemic control, insulin sensitivity, gestational weight change, maternal postpartum BMI, macrosomia, LGA, birthweight, gestational age at birth, postpartum development of diabetes mellitus
Notes	GDM diagnosis based on 3-h 75 grams OGTT, bloods taken every 30 min; GDM was defined as 2 or more plasma glucose samples above three standard deviations of the mean

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Reported as "the randomisation was performed block-wise stratified for pre-pregnancy weight with an expected ratio of obese to normal weight of three to one.The block sizes were six and two in the two strata"
Allocation concealment (selection bias)	Low risk	Reported as that "the randomisation was performed by a third person at an independent centre outside our institution, which produced information about the outcome of randomisation at baseline measurement in week 33"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It was not feasible to blind study participants. No information on whether research personnel were blinded or not

Lauszus 2001 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data were missing at multiple collection points for 1 to 2 patients but this was explained in the text and is unlikely to affect the results for perinatal outcomes
Selective reporting (reporting bias)	High risk	Most of the prespecified review outcomes were not reported in this trial
Other bias	High risk	Women in the high-monounsaturated fat diet group had a higher trial entry BMI (mean [SD]: 35 [2.4] kg/m^2) when compared with women in the high-carbohydrate group (mean [SD]: 32.2 [1.5] kg/m^2).

Louie 2011

Methods	Randomised controlled trial.
Participants	N = 92. Women aged at 18-45 years, diagnosed with GDM by a 75 g OGTT between 20 and 32 weeks' gestation according to ADIPS criteria (see notes), with an otherwise healthy singleton pregnancy Exclusion criteria: women who had special dietary requirements (including vegetarianism/veganism), pre-existing diabetes, or pregnancy achieved by assisted reproduction and those who smoked or consumed alcohol during pregnancy Setting: Australia.
Interventions	Low-GI diet group (n = 50): diet GI target of ≤ 50, other nutrients were the same as the comparison group High-fibre moderate-GI diet (n = 49): diet GI target of around 60, which represented average GI of Australian population All women: 1. healthy diets of similar protein (15% to 25% total daily energy intake), fat (25% to 30% total daily energy intake), and carbohydrate (40% to 45% total daily energy intake) content; 2. completed 3-day food record (2 weekdays and 1 weekend day) at baseline and 36-37 weeks' gestation; 3. received 2 food model booklet to assist in portion size estimation.
Outcomes	Pregnancy outcomes: birthweight, the need for emergency caesarean section, gestational age at birth, macrosomia, SGA, LGA, ponderal index, neonatal anthropometry (length, head circumference), maternal metabolic profile in GDM
Notes	1. 68% participants in this trial had a BMI < 25 kg/m^2. 2. Insulin treatment was commenced if the mean fasting BGL or 1-h postprandial BGL in the preceding week exceeded 5.2 and 7.5 mmol/L, respectively.

	3. Self-reported pre-pregnancy weight; last weight before delivery was obtained from medical record. 4. ADIPS criteria used for GDM diagnosis: • fasting BGL ≥ 5.5 mmol/L; • 2-hour BGL after 75 g glucose load ≥ 8.0 mmol/L; • 1 or more value(s) is (are) met or exceeded.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Described as "the enrolled subjects were centrally randomised to study diet by computer generated random numbers, stratified by BMI and weeks of gestation"
Allocation concealment (selection bias)	Low risk	Described as "the allocation sequence was unpredictable and concealed from the recruiter"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Reported that (besides research dietitian who provided trial intervention) all study personnel and participants were blinded to dietary assignment
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Reported that the unblinded research dietitian was involved in data collection, no other information on whether or not other outcome assessors were blinded to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	In the low-GI group, 1 woman was excluded due to incorrect GDM diagnosis, 3 women withdraw after intervention, 2 women had preterm births, leaving 44 women who completed the study, and 47 women were included in analysis In high-fibre group, 2 women withdrew after group allocation, another 2 women withdrew after intervention; 2 women had preterm births, leaving 43 women who completed the study and 45 women who were included in analysis
Selective reporting (reporting bias)	High risk	Only limited data were reported on some of the prespecified review outcomes
Other bias	High risk	At baseline, 2-hour post 75 g glucose load BGL for women in low-GI group were significantly higher than those in conventional high-fibre group (mean [SD]: low-GI 8.6 [1.2] mmol/L vs high-fibre group 8.0 [1.3] mmol/L; P = 0.024)

Magee 1990

Methods	Randomised controlled trial.
Participants	N = 12. Obese women (defined as: pre-pregnancy weight > 120% of ideal body weight as specified by the Corrected 1959 Metropolitan Life Insurance table) with GDM according to ADA criteria (see notes) Exclusion criteria: not reported. Setting: the United States.
Interventions	During the second hospitalised week: Energy-restricted diet group (n = 7): on an energy-restricted diet of 1200 kcal/day diet by reducing serving size without changing the pattern and content of the diet in the first hospitalised week No energy restriction diet group (n = 5): continue the standard diet prescribed as the first week, for about 2400 kcal/day All women: hospitalised for the 2 weeks duration. Studies and diet during the first week were identical for all patients During the first hospitalised week: 1. dietary pattern: 25% total energy for breakfast, lunch and dinner. 12.5% total energy for afternoon tea and supper; 2. diet contents were: 50% carbohydrate, 30% fat, 20% protein, with 11 g of total dietary fibre per 500kcal; 3. daily morning double-voided urine sample for ketone and fasting plasma glucose; 4. on the sixth day of each week: blood after overnight fast for plasma glucose, insulin, triglyceride, free fatty acids, glycerol, β-hydroxhbutyrate. A glucose profile with 25 samples drawn over 24 hrs was initiated as well on the same day; 5. on the seventh day of each week: repeat fasting blood work as day 6 and a 3-h 100-g OGTT.
Outcomes	Metabolic profile including plasma glucose, fasting plasma insulin, urine ketones
Notes	ADA criteria used for GDM diagnosis: • 2 or more values meeting the following in 100g 3-h OGTT; • fasting 5.3 mmol/L; • 1-h: 10 mmol/L; • 2-h: 8.6 mmol/L; • 3-h: 7.8 mmol/L.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as "subjects were randomised to the control or calorie-restricted group"
Allocation concealment (selection bias)	Unclear risk	No information was given on allocation concealment.

Magee 1990 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information on whether participants or research personnel were blinded or not
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up or post randomisation exclusions reported
Selective reporting (reporting bias)	High risk	None of the clinical outcomes prespecified in this review was reported
Other bias	Low risk	There is no obvious risk of other bias.

Moses 2009

Methods	Randomised controlled trial.
Participants	N = 63. Women aged at 18 to 40 years (inclusive) diagnosed with GDM according to ADIPS criteria (see notes), singleton pregnancy, no previous GDM, non-smoker, and seen for the first dietary visit between 28 and 32 weeks of gestation, and ability to follow the protocol requirements Exclusion criteria: any condition or medication that could affect glucose levels and unwillingness to follow the prescribed diet Setting: Australia.
Interventions	Low-GI diet group (n = 31): diet based on previously verified low-glycaemic index food, including pasta, grain breads, and unprocessed breakfast cereals with a high-fibre content. Women were specifically asked to avoid consuming white bread, processed commercial breakfast cereals, potatoes, and some rice varieties Conventional high-fibre, low-sugar, higher-GI diet group (n = 32): women were advised to follow a diet with a high-fibre and low-sugar content, with no specific mention of the GI. Potatoes, whole wheat bread, and specific high-fibre, moderate-to-high GI breakfast cereals were recommended All women: 1. were provided with a home glucose meter and were asked to test after fasting and 1 hour after the start of each of their 3 major meals at least every second day; 2. had at least 4 times diabetes centre visit with dietitian for dietary assessment and if they required insulin were seen as many times as necessary for insulin adjustment; 3. were provided with a booklet outlining the carbohydrate choices the carbohydrate food amounts constituting 1 serving (based on 15 g portions); 4. were advised to consume 3 small meals and 2 to 3 snacks with a specified number of servings of carbohydrate.

Moses 2009 (*Continued*)

Outcomes	Method of delivery, macrosomia, LGA, induction of labour, preterm birth, birthweight, infant anthropometric outcomes, Apgar score
Notes	ADIPS criteria used for GDM diagnosis: • fasting BGL ≥ 5.5 mmol/L; • 2-hour BGL after 75 g glucose load ≥ 8.0 mmol/L; • 1 or more value(s) is (are) met or exceeded.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Described as: "participants were randomly assigned to receive one of two different diets using permuted blocks of unequal size with the list generated using STATA (Version 7.0)"
Allocation concealment (selection bias)	Low risk	Method of generation of randomisation sequence likely to have concealed allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants and study dietitian were not blinded. The physician caring for the patients was blinded to group allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up or post randomisation exclusion.
Selective reporting (reporting bias)	High risk	Most of the prespecified review outcomes were not reported in this trial
Other bias	Low risk	There is no obvious risk of other bias.

Rae 2000

Methods	Randomised controlled trial.
Participants	N = 125; N = 117 women involved in analysis (8 withdraw). Women at ≤ 35 weeks 6 days gestation; > 110% of ideal body weight for height (adjusted for expected pregnancy weight gain and using a BMI of 25 as equal to 100% ideal body weight); fasting BGL > 5.4 mmol/L and or 2 hour BGL > 7.9 mmol/L in 75 g 2 hour OGTT Exclusion criteria: not reported. Setting: Australia.

Interventions	Energy-restricted diet group (30% energy restriction) (n = 67 with outcome data available for 63 women): women on a diabetic diet providing between 6800 and 7600 kJ energy per day, which represented 70% of the Recommended Dietary Intake for pregnancy women (National Health and Medical Research Council of Australia) No energy restriction diet group (n = 58 with outcome data available for 54 women): women on diabetic diet without energy restriction, providing 8600 to 9500 kJ energy per day All women: 1. diabetes education provided by a research dietitian at each antenatal visit; 2. hyperglycaemia control, BGL self-monitoring: before and 2 hours after each meal (6 times per day), for a minimum of 2 days each week; 3. fetal and maternal surveillance and anticipated term delivery; 4. use of insulin decided by medical staffs that were blinded to group allocation. Criteria for insulin: fasting BGL > 5.5 mmol/L or 2-h BGL > 7.0 mmol/L on two or more occasions in any 72 hours period at the same pre- or post-prandial epoch; 5. metabolic monitoring for HbA1c, serum beta-hydroxybutyrate, urinary ketone; 6. 3-day food intake dairies for adherence to diet.
Outcomes	Macrosomia, newborns anthropometric measurement at 5 days of age, maternal dietary intake
Notes	• Women's BMI at GDM diagnosis mean [SD] was 37.9 [0.7] and 38.9 [0.7] for women in intervention group and control group, respectively. • Due to the adherence to the dietary intervention, there was no significant difference in total energy intake between groups. • 7 sets of twins were included in the study, 3 sets in the intervention group and 4 sets in the control group.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Described as "women were allocated at random by draw of opaque numbered envelopes"
Allocation concealment (selection bias)	Unclear risk	Described as above. It is likely adequately done.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants and diabetes service staff were blinded to allocation to diet group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Described as that "demographic, obstetric and neonatal data were collected prospectively'. No information on whether or not outcome assessors were blinded to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	A total of 8 women (6.4%) (four from each group) withdrew and were excluded from data analysis; reasons for withdraw and baseline details about these eight women

		were not given Some data points have small numbers of lost participants that are unexplained in the text, although this is unlikely to have affected the overall results.
Selective reporting (reporting bias)	High risk	Most of the prespecified review outcomes were not reported in this trial Outcomes including shoulder dystocia, birthweight, gestational age at birth were reported in one trial. However, as it was unclear about the sample sizes in each study groups for each of these reported outcomes, hence, no data were able to be included in the review
Other bias	Low risk	There is no obvious risk of other bias.

Reece 1995

Methods	Randomised controlled trial.
Participants	N = 22. Women diagnosed with GDM between 24-29 weeks' gestation. Exclusion criteria: diagnosis of GDM after 29 weeks' gestation Setting: United States.
Interventions	ADA diet group (n = 11): diet containing 20 g fibre per day; 30% daily energy intake derived from fat, and 50% derived from carbohydrate Fibre-enriched diet group (n = 11): diet containing 80 g fibre per day; 20% daily energy intake derived from fat, and 60% derived from carbohydrate All women: capillary BGL 6 times a day (before and after each meal), twice weekly
Outcomes	Gestational weight gain, insulin required for hyperglycaemia, birthweight, gestational age at birth
Notes	GDM diagnostic criteria not reported.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation was done by using a random numbers table.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants were unlikely to be blinded. The research dietitian and the diabetes nurse specialist who were responsible for monitoring diet compliance

Reece 1995 (*Continued*)

		and glycaemic control were unlikely to be blinded Unclear about whether other research personnel were blinded or not
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Women with insulin-dependent diabetes and GDM were included in the trial. It was reported that 11/61 women (5 in the ADA diet group and 6 in the fibre-enriched diet) were excluded from the study after randomisation: one had a spontaneous abortion, 2 moved away, and 4 from each group were noncompliant It is unclear how many of these 11 women excluded after randomisation were women with GDM
Selective reporting (reporting bias)	High risk	Most of the prespecified review outcomes were not reported in this trial
Other bias	Low risk	There is no obvious risk of other bias.

ADA: the American Diabetes Association
ADIPS: Australian Diabetes in Pregnancy Society
CDA: Canadian Diabetes Association
BGL: blood glucose level
BMI: body mass index
GDM: gestational diabetes mellitus
GI: glycaemic index
HBGM: home blood glucose monitoring
LGA: large-for-gestational age
NIPerIER: National Institute of Perinatology Isidro Espinosa de los Reyes
OGTT: oral glucose tolerance test
SD: standard deviation
SGA: small-for-gestational age
SMBG: self-monitored blood glucose
T1DM: type 1 diabetes mellitus
WHO: World Health Organization

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Gillen 2004	Study compared standard clinical care only for women with GDM with standard clinical care with additional advice targeting intakes of foods rich in unsaturated fats
Gillmer 1986	Study compared diet alone with diet and insulin for GDM management, did not meet the inclusion criteria of this review for interventions
Ilic 1999	Women in one group had a meal containing saturated fat and women in the other group had a meal containing monounsaturated fat. 2 weeks later, women in the 2 groups swapped to have the other group's meal Not meeting the inclusion criteria for eligible interventions for this review
Knopp 1991	A literature review on management of GDM.
Ma 2011	Participants were also instructed to increase exercise level by adding daily walking activity
Nolan 1984	A randomised cross-over study.
Reader 2006	Trial did not compare different types of dietary advice, but compared different types of care for women with GDM. Women in the intervention group were cared according to the nutrition practice guidelines for GDM, that emphasised 3 major areas of setting individualised medical nutrition therapy goals, BGL monitoring, a minimum of 3 nutrition visits with follow ups via phone or in person. Women in the control group received usual prenatal nutrition care

BGL: blood glucose level
GDM: gestational diabetes mellitus

DATA AND ANALYSES

Comparison 1. Low-moderate GI food versus high-moderate food

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Macrosomia (birthweight greater than 4000 g)	2	89	Risk Ratio (M-H, Fixed, 95% CI)	0.45 [0.10, 2.08]
2 Large-for-gestational age (birthweight ≥ 90th percentile for gestational age)	2	89	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.27, 3.36]
3 Caesarean section	1	63	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.29, 1.47]
4 Operative vaginal birth	1	63	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.16, 2.37]
5 Normal vaginal birth	1	63	Risk Ratio (M-H, Fixed, 95% CI)	1.35 [0.89, 2.07]
6 Birthweight (g)	1	62	Mean Difference (IV, Fixed, 95% CI)	-50.70 [-272.56, 171.16]
7 Gestational age at birth	1	62	Mean Difference (IV, Fixed, 95% CI)	0.30 [-0.30, 0.90]
8 Small-for-gestational age	1	63	Risk Ratio (M-H, Fixed, 95% CI)	5.16 [0.26, 103.27]
9 Induction of labour	1	63	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.33, 2.34]
10 Preterm birth (< 37 weeks' gestation)	1	63	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.05, 5.41]
11 Insulin or oral hypoglycaemic agent required for hyperglycaemia	3	126	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.37, 1.93]

Comparison 2. Low-GI diet versus high-fibre moderate-GI diet

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Macrosomia (birthweight greater than 4000 g)	1	92	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.03, 2.96]
2 Large-for-gestational age (birthweight ≥ 90th percentile for gestational age)	1	92	Risk Ratio (M-H, Fixed, 95% CI)	2.87 [0.61, 13.50]
3 Caesarean section	1	88	Risk Ratio (M-H, Fixed, 95% CI)	1.8 [0.66, 4.94]
4 Birthweight (g)	1	92	Mean Difference (IV, Fixed, 95% CI)	0.0 [-277.18, 277.18]
5 Gestational age at birth (weeks)	1	92	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.39, 0.19]
6 Preterm birth	1	92	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.14, 6.51]
7 Small-for-gestational age	1	92	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.34, 4.18]
8 Ponderal index (kg/m^3)	1	92	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.79, 1.19]
9 Weight gain during pregnancy (kg)	1	87	Mean Difference (IV, Fixed, 95% CI)	-1.20 [-3.43, 1.03]
10 Adherence to dietary intervention	1	92	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.64, 1.11]

11 Insulin required for hyperglycaemia	1	92	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.58, 1.17]

Comparison 3. Energy-restricted diet versus no energy restriction diet

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Fetal mortality	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Macrosomia	1	122	Risk Ratio (M-H, Fixed, 95% CI)	1.56 [0.61, 3.94]
3 Large-for-gestational age	1	123	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.65, 2.12]
4 Caesarean section	1	121	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.74, 1.89]
5 Operative vaginal birth	1	121	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.38, 2.54]
6 Normal vaginal birth	1	121	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.63, 1.27]
7 Induction of labour	1	114	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.68, 1.53]
8 Pre-eclampsia	1	117	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.51, 1.97]
9 Insulin or oral hypoglycaemic agent required for hyperglycaemia	1	117	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.47, 2.34]
10 Insulin sensitivity	1		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1 Fasting plasma glucose (mmol)	1	12	Std. Mean Difference (IV, Fixed, 95% CI)	-0.35 [-1.51, 0.81]
10.2 Fasting plasma insulin (pM)	1	12	Std. Mean Difference (IV, Fixed, 95% CI)	-0.17 [-1.32, 0.98]

Comparison 4. Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Macrosomia (birthweight greater than 4000 g)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Caesarean section	1	30	Risk Ratio (M-H, Fixed, 95% CI)	1.4 [0.57, 3.43]
3 Operative vaginal birth	1	30	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.07, 14.55]
4 Normal vaginal birth	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.39, 1.54]
5 Birthweight (g)	1	30	Mean Difference (IV, Fixed, 95% CI)	22.0 [-241.06, 285.06]
6 Gestational age at birth (weeks)	1	30	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.83, 1.03]

Comparison 5. High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Macrosomia (birthweight greater than 4000 g)	1	27	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.19, 2.18]
2 Large-for-gestational age	1	27	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.21, 1.37]
3 Birthweight (g)	1	27	Mean Difference (IV, Fixed, 95% CI)	1.0 [-112.85, 114.85]
4 Gestational age at birth (weeks)	1	27	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.13, 0.33]
5 Pre-eclampsia	1	27	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Insulin or oral hypoglycaemic agent required for hyperglycaemia	1	27	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Maternal weight at late pregnancy (third trimester) (kg)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Maternal weight at 36 weeks' gestation	1	27	Mean Difference (IV, Fixed, 95% CI)	12.60 [7.93, 17.27]
7.2 Maternal weight at 38 weeks' gestation	1	27	Mean Difference (IV, Fixed, 95% CI)	11.80 [7.23, 16.37]
7.3 Maternal weight at delivery	1	27	Mean Difference (IV, Fixed, 95% CI)	11.90 [7.47, 16.33]
8 Maternal BMI at late pregnancy (third trimester) (kg/m^2)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
8.1 Maternal BMI at 36 weeks' gestation (kg/m^2)	1	27	Mean Difference (IV, Fixed, 95% CI)	4.70 [3.18, 6.22]
8.2 Maternal BMI at 38 weeks' gestation (kg/m^2)	1	27	Mean Difference (IV, Fixed, 95% CI)	3.80 [2.22, 5.38]
8.3 Maternal BMI at delivery (kg/m^2)	1	27	Mean Difference (IV, Fixed, 95% CI)	3.90 [2.41, 5.39]
9 Maternal postpartum BMI (> 4 months postpartum) (kg/m^2)	1	27	Mean Difference (IV, Fixed, 95% CI)	4.10 [2.34, 5.86]
10 Development of type 2 diabetes	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
10.1 Diagnosed by OGTT at early postnatal period (within 6 weeks postpartum)	1	24	Risk Ratio (M-H, Fixed, 95% CI)	2.0 [0.45, 8.94]
10.2 Diagnosed by OGTT at ≥ 4 months postpartum	1	6	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.10, 9.61]
11 Development of glucose intolerance without meeting type 2 diabetes diagnostic criteria	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
11.1 Diagnosed by OGTT at early postnatal period (within 6 weeks postpartum)	1	24	Risk Ratio (M-H, Fixed, 95% CI)	1.5 [0.30, 7.43]
11.2 Diagnosed by OGTT at ≥ 4 months postpartum	1	7	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.01, 4.93]

Comparison 6. Standard ADA diet (20 g fibre/day) versus fibre-enriched diet (80 g fibre/ day)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Birthweight (g)	1	22	Mean Difference (IV, Fixed, 95% CI)	-94.0 [-446.71, 258.71]
2 Gestational age at birth (weeks)	1	22	Mean Difference (IV, Fixed, 95% CI)	0.0 [-1.30, 1.30]
3 Insulin or oral hypoglycaemic agent required for hyperglycaemia	1	22	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Gestational weight gain (kg)	1	22	Mean Difference (IV, Fixed, 95% CI)	2.40 [-2.20, 7.00]

Analysis 1.1. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 1 Macrosomia (birthweight greater than 4000 g).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 1 Macrosomia (birthweight greater than 4000 g)

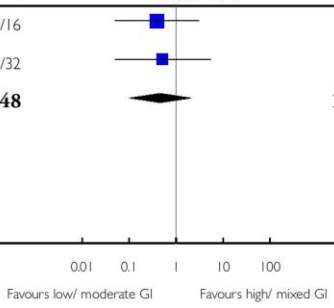
Study or subgroup	Low/ moderate GI diet n/N	High/ mixed GI diet n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Grant 2011	1/10	4/16		61.0 %	0.40 [0.05, 3.09]
Moses 2009	1/31	2/32		39.0 %	0.52 [0.05, 5.41]
Total (95% CI)	**41**	**48**		**100.0 %**	**0.45 [0.10, 2.08]**

Total events: 2 (Low/ moderate GI diet), 6 (High/ mixed GI diet)

Heterogeneity: $Chi^2 = 0.03$, df = 1 (P = 0.87); $I^2 = 0.0\%$

Test for overall effect: Z = 1.03 (P = 0.30)

Test for subgroup differences: Not applicable

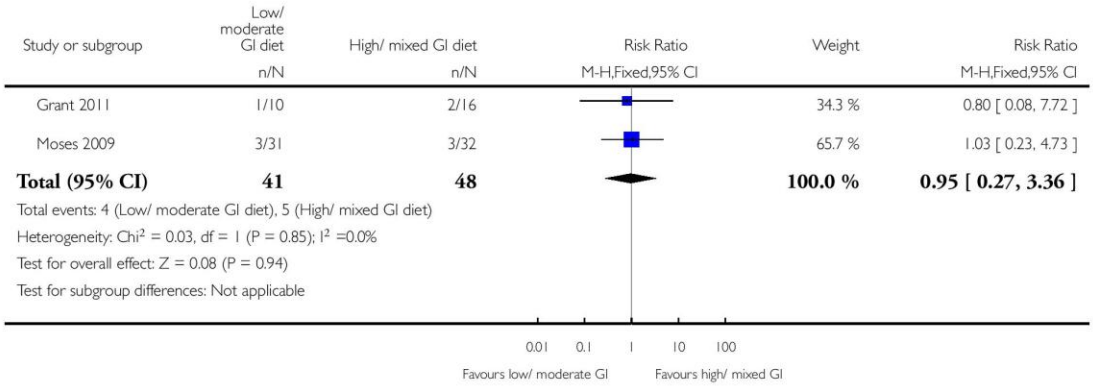


Analysis 1.2. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 2 Large-for-gestational age (birthweight ≥ 90th percentile for gestational age).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 2 Large-for-gestational age (birthweight ≥ 90th percentile for gestational age)

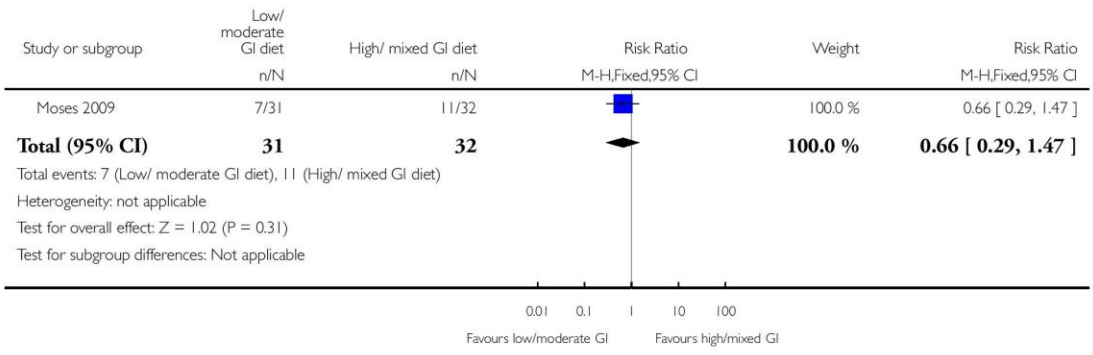


Analysis 1.3. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 3 Caesarean section.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 3 Caesarean section

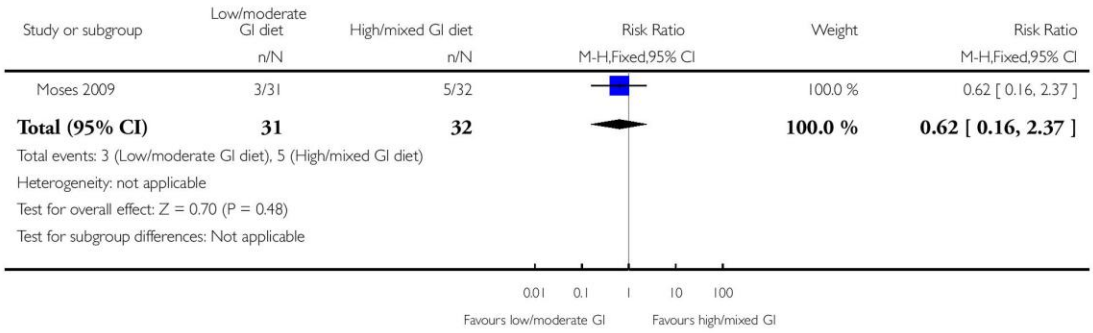


Analysis 1.4. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 4 Operative vaginal birth.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 4 Operative vaginal birth

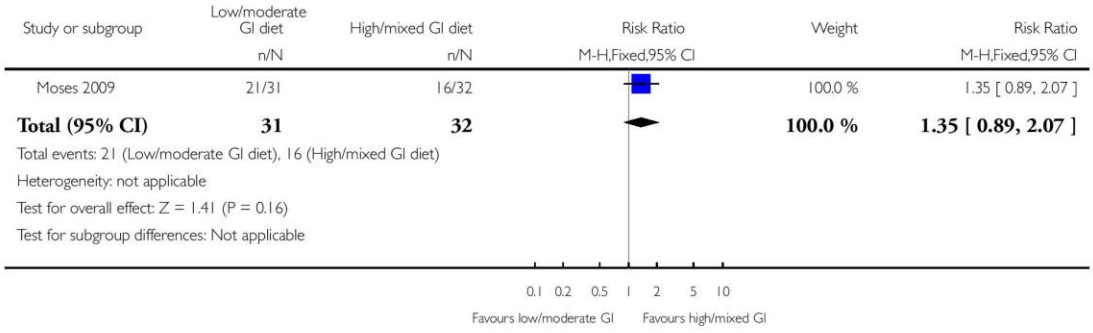


Analysis 1.5. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 5 Normal vaginal birth.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 5 Normal vaginal birth

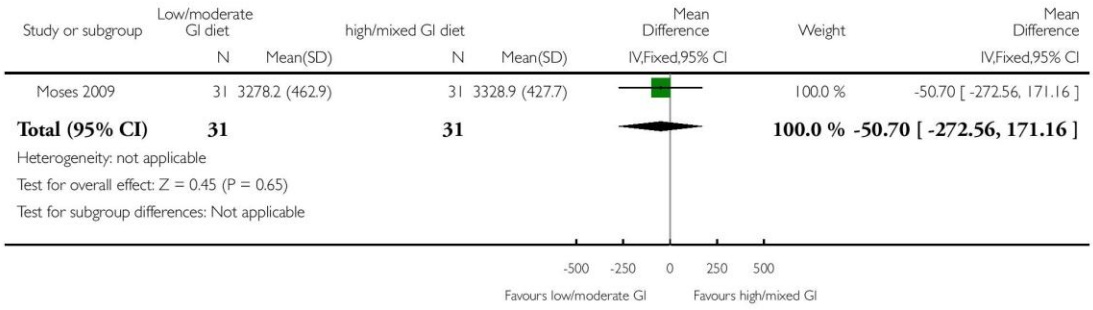


Analysis 1.6. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 6 Birthweight (g).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 6 Birthweight (g)

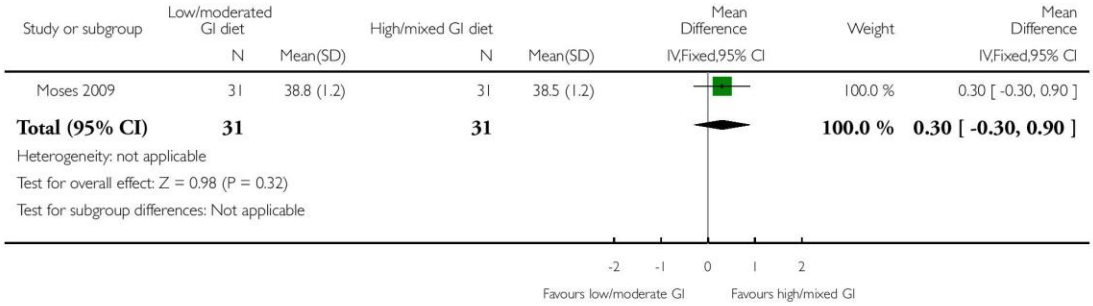


Analysis 1.7. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 7 Gestational age at birth.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 7 Gestational age at birth

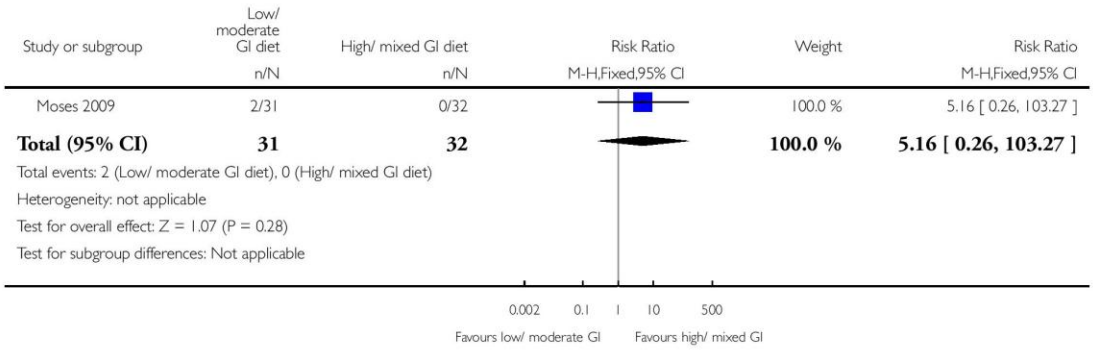


Analysis 1.8. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 8 Small-for-gestational age.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 8 Small-for-gestational age

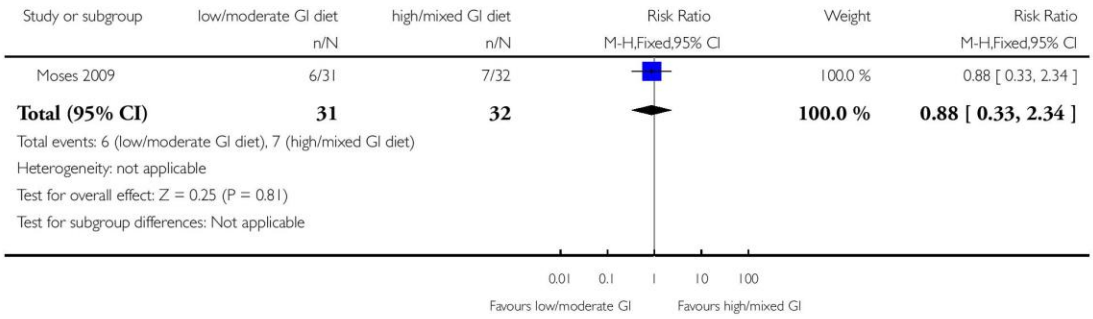


Analysis 1.9. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 9 Induction of labour.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 9 Induction of labour

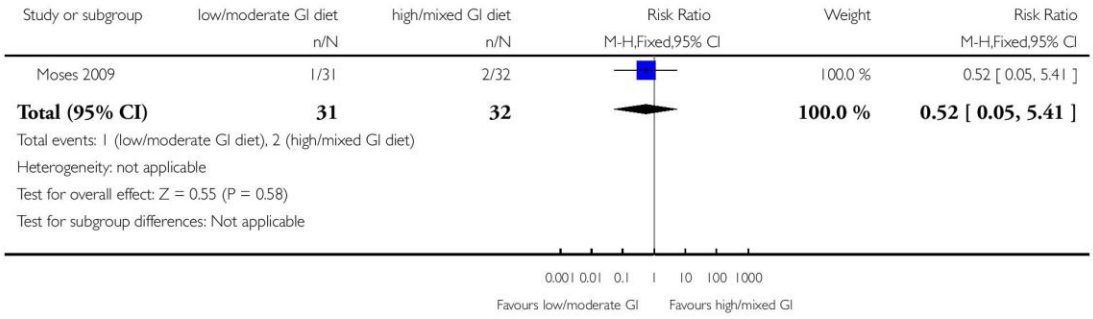


Analysis 1.10. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 10 Preterm birth (< 37 weeks' gestation).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 10 Preterm birth (< 37 weeks' gestation)

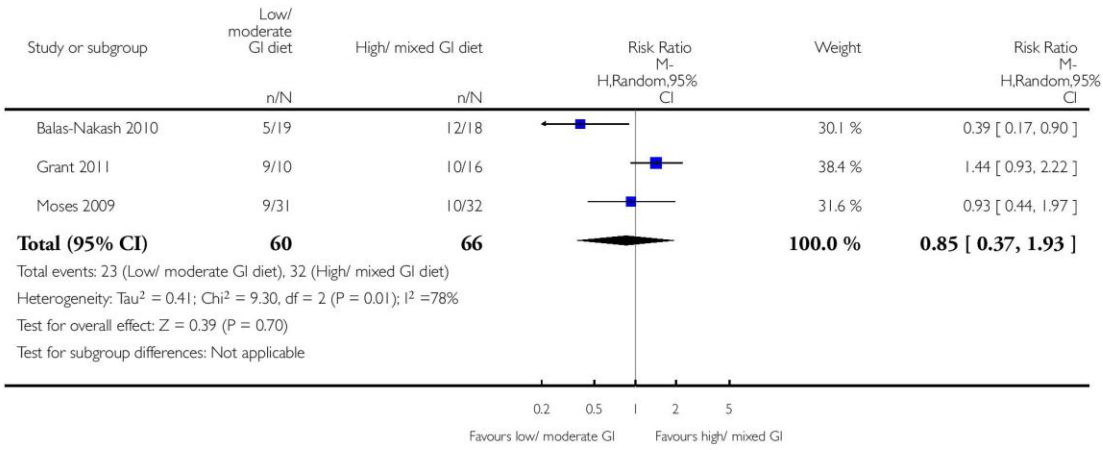


Analysis 1.11. Comparison 1 Low-moderate GI food versus high-moderate food, Outcome 11 Insulin or oral hypoglycaemic agent required for hyperglycaemia.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 1 Low-moderate GI food versus high-moderate food

Outcome: 11 Insulin or oral hypoglycaemic agent required for hyperglycaemia

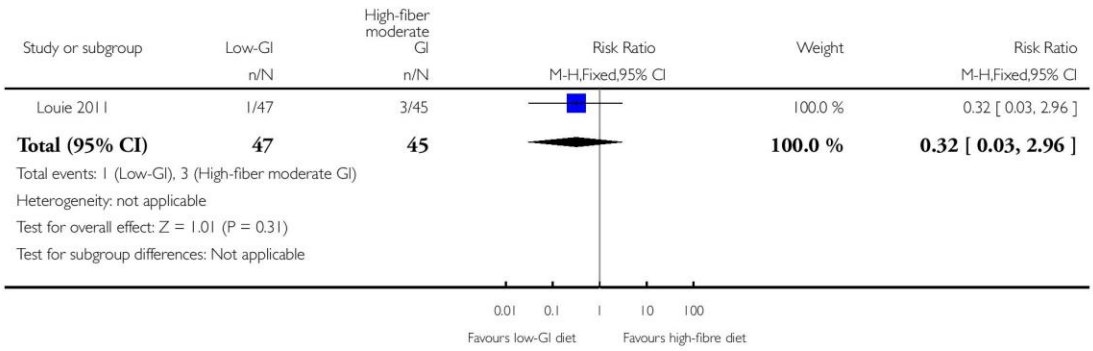


Analysis 2.1. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 1 Macrosomia (birthweight greater than 4000 g).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 1 Macrosomia (birthweight greater than 4000 g)

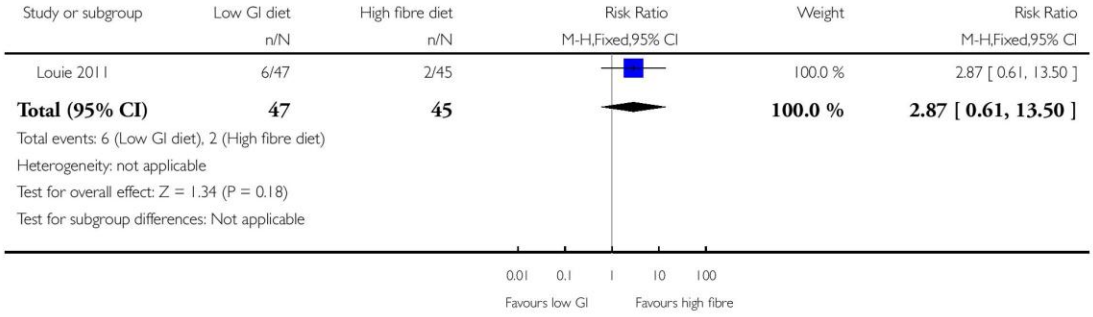


Analysis 2.2. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 2 Large-for-gestational age (birthweight ≥ 90th percentile for gestational age).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 2 Large-for-gestational age (birthweight ≥ 90th percentile for gestational age)

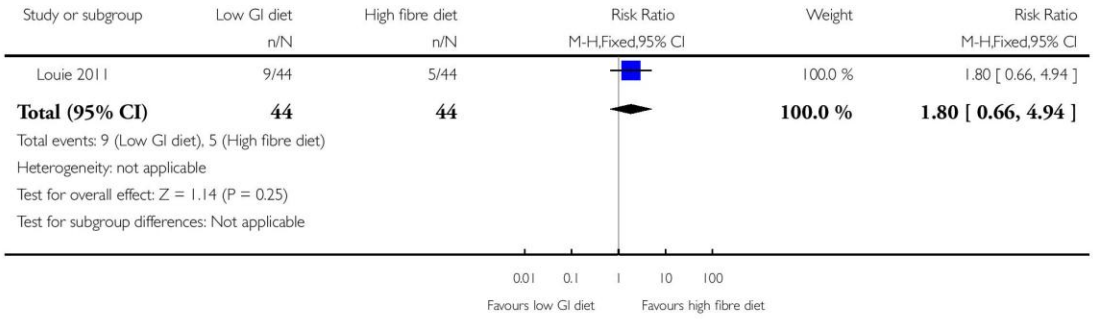


Analysis 2.3. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 3 Caesarean section.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 3 Caesarean section

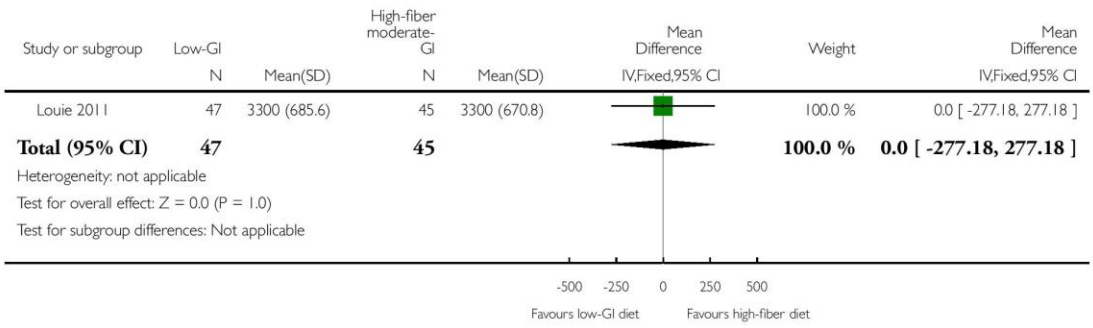


Analysis 2.4. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 4 Birthweight (g).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 4 Birthweight (g)

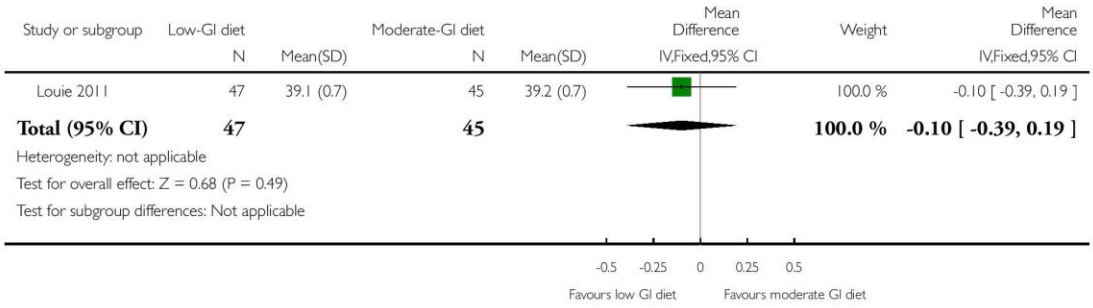


Analysis 2.5. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 5 Gestational age at birth (weeks).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 5 Gestational age at birth (weeks)

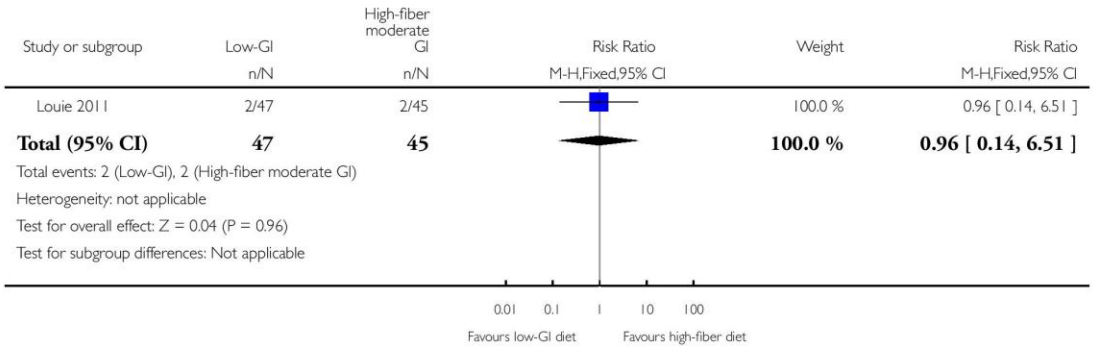


Analysis 2.6. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 6 Preterm birth.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 6 Preterm birth

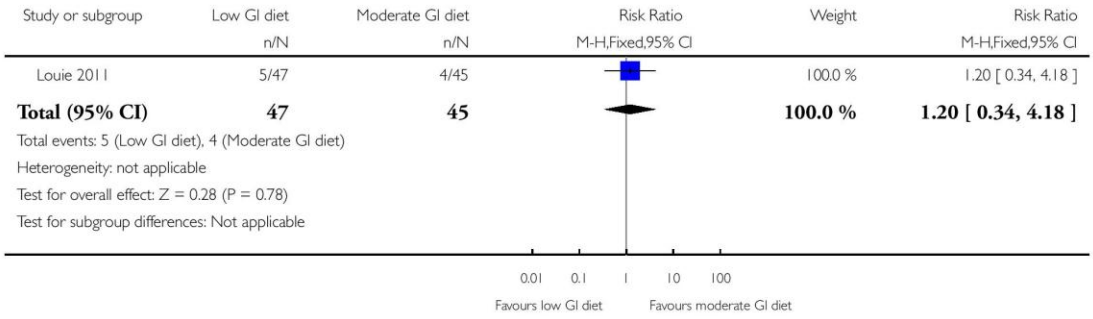


Analysis 2.7. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 7 Small-for-gestational age.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 7 Small-for-gestational age

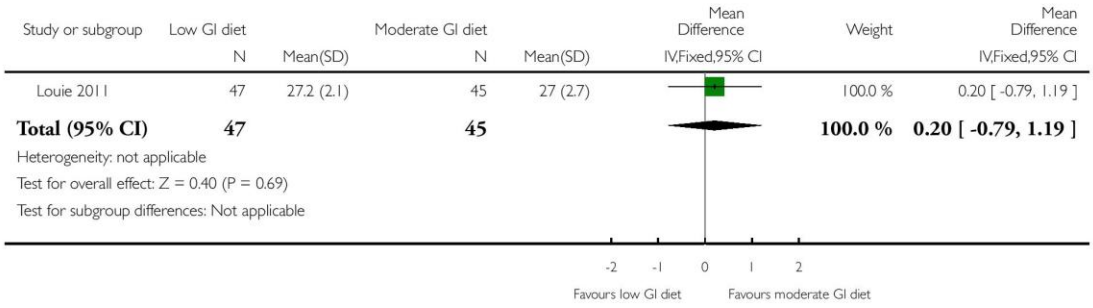


Analysis 2.8. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 8 Ponderal index (kg/m3).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 8 Ponderal index (kg/m^3)

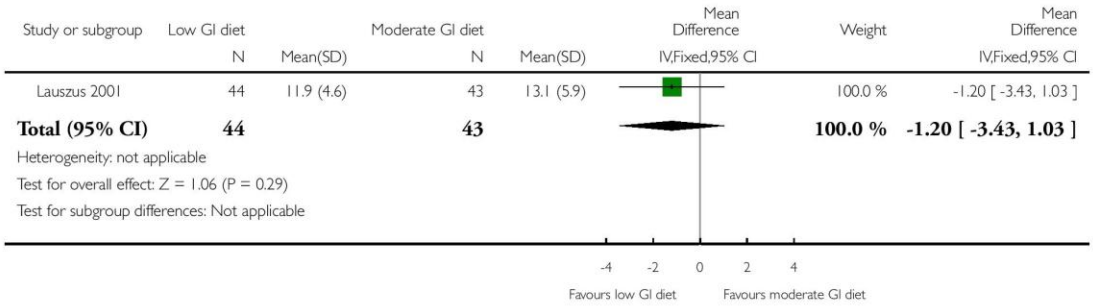


Analysis 2.9. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 9 Weight gain during pregnancy (kg).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 9 Weight gain during pregnancy (kg)

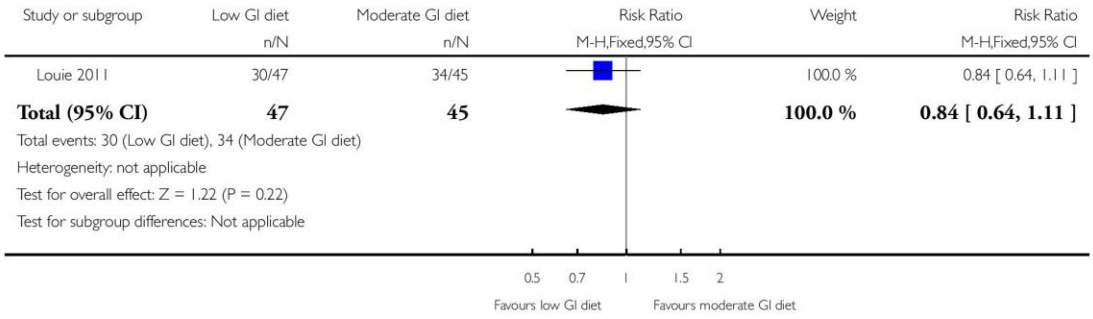


Analysis 2.10. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 10 Adherence to dietary intervention.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 10 Adherence to dietary intervention



Analysis 2.11. Comparison 2 Low-GI diet versus high-fibre moderate-GI diet, Outcome 11 Insulin required for hyperglycaemia.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 2 Low-GI diet versus high-fibre moderate-GI diet

Outcome: 11 Insulin required for hyperglycaemia

Study or subgroup	Low-GI n/N	High-fiber moderate GI n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Louie 2011	25/47	29/45		100.0 %	0.83 [0.58, 1.17]
Total (95% CI)	**47**	**45**		**100.0 %**	**0.83 [0.58, 1.17]**
Total events: 25 (Low-GI), 29 (High-fiber moderate GI)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.09 (P = 0.28)					
Test for subgroup differences: Not applicable					

Analysis 3.1. Comparison 3 Energy-restricted diet versus no energy restriction diet, Outcome 1 Fetal mortality.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 3 Energy-restricted diet versus no energy restriction diet

Outcome: 1 Fetal mortality

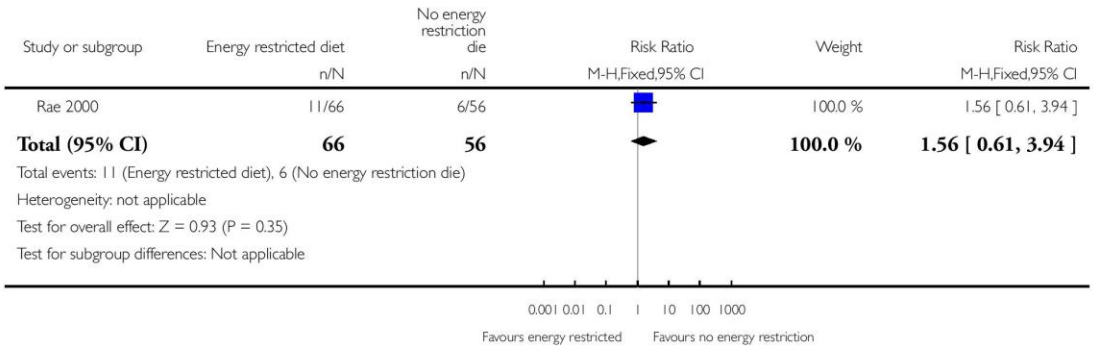
Study or subgroup	Energy restricted diet n/N	No energy restriction die n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Rae 2000	0/66	0/58		0.0 [0.0, 0.0]
Total (95% CI)	**66**	**58**		**0.0 [0.0, 0.0]**
Total events: 0 (Energy restricted diet), 0 (No energy restriction die)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Test for subgroup differences: Not applicable				

Analysis 3.2. Comparison 3 Energy-restricted diet versus no energy restriction diet, Outcome 2 Macrosomia.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 3 Energy-restricted diet versus no energy restriction diet

Outcome: 2 Macrosomia

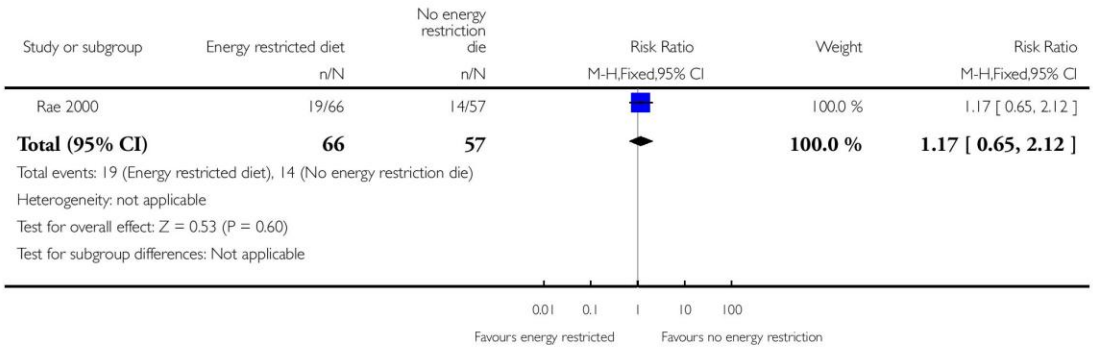


Analysis 3.3. Comparison 3 Energy-restricted diet versus no energy restriction diet, Outcome 3 Large-for-gestational age.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 3 Energy-restricted diet versus no energy restriction diet

Outcome: 3 Large-for-gestational age

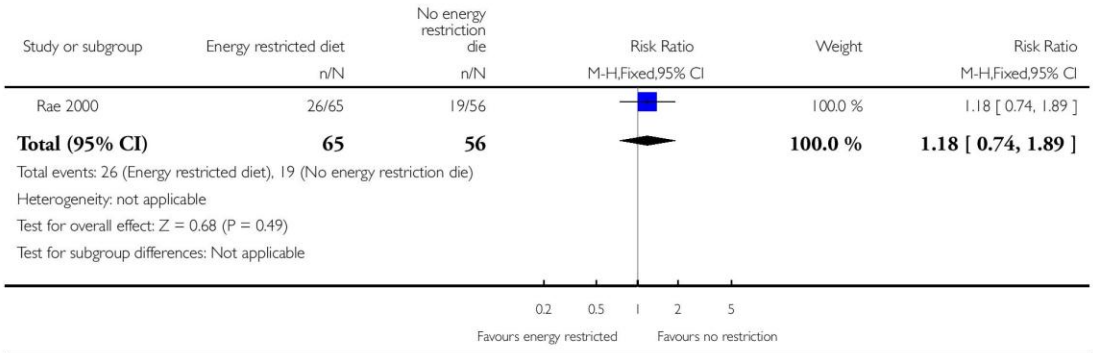


Analysis 3.4. Comparison 3 Energy-restricted diet versus no energy restriction diet, Outcome 4 Caesarean section.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 3 Energy-restricted diet versus no energy restriction diet

Outcome: 4 Caesarean section

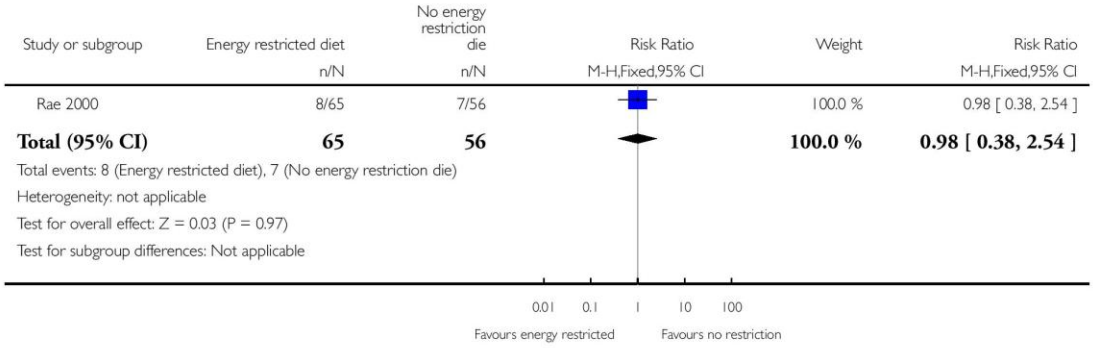


Analysis 3.5. Comparison 3 Energy-restricted diet versus no energy restriction diet, Outcome 5 Operative vaginal birth.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 3 Energy-restricted diet versus no energy restriction diet

Outcome: 5 Operative vaginal birth

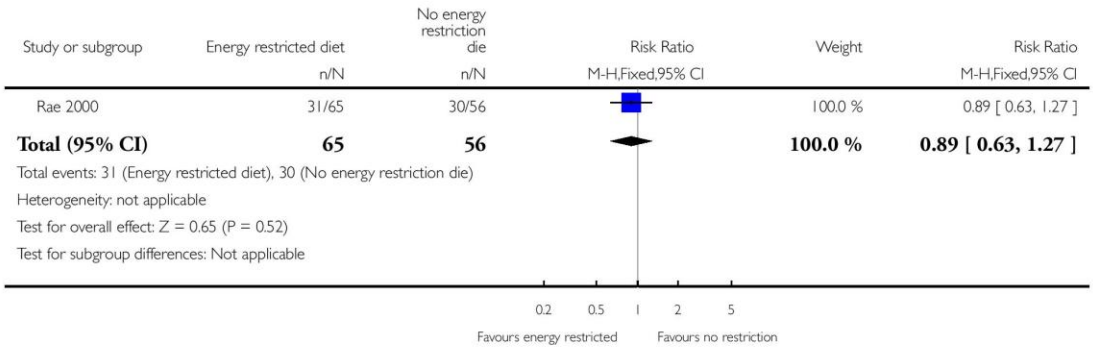


Analysis 3.6. Comparison 3 Energy-restricted diet versus no energy restriction diet, Outcome 6 Normal vaginal birth.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 3 Energy-restricted diet versus no energy restriction diet

Outcome: 6 Normal vaginal birth

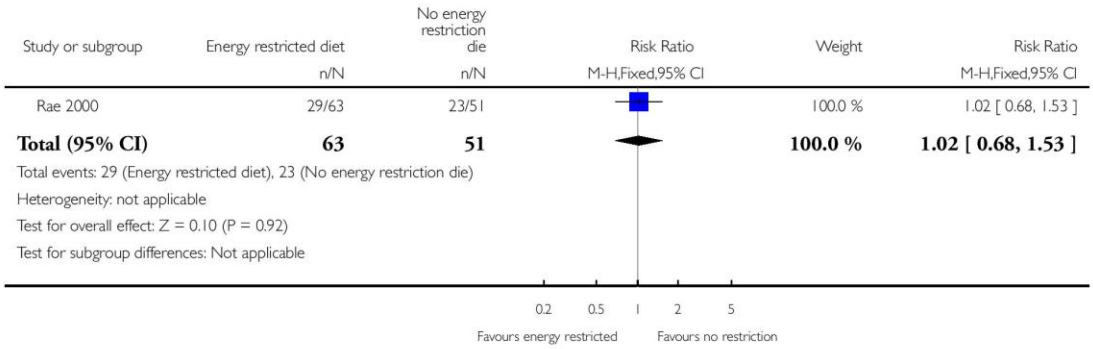


Analysis 3.7. Comparison 3 Energy-restricted diet versus no energy restriction diet, Outcome 7 Induction of labour.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 3 Energy-restricted diet versus no energy restriction diet

Outcome: 7 Induction of labour

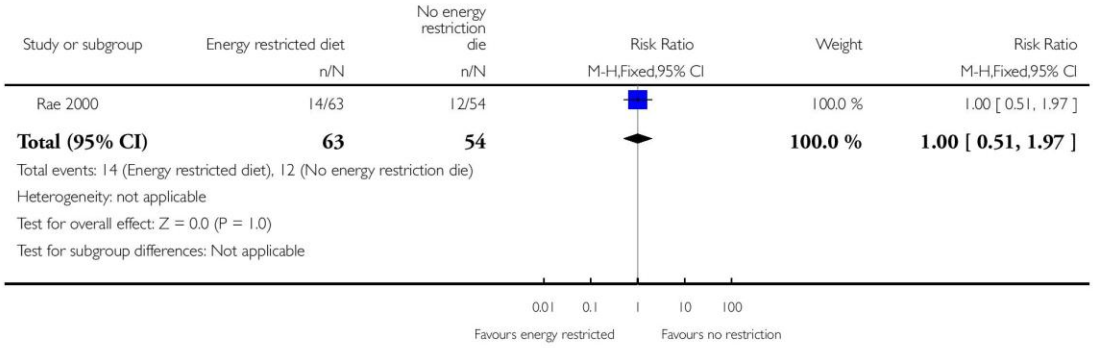


Analysis 3.8. Comparison 3 Energy-restricted diet versus no energy restriction diet, Outcome 8 Pre-eclampsia.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 3 Energy-restricted diet versus no energy restriction diet

Outcome: 8 Pre-eclampsia

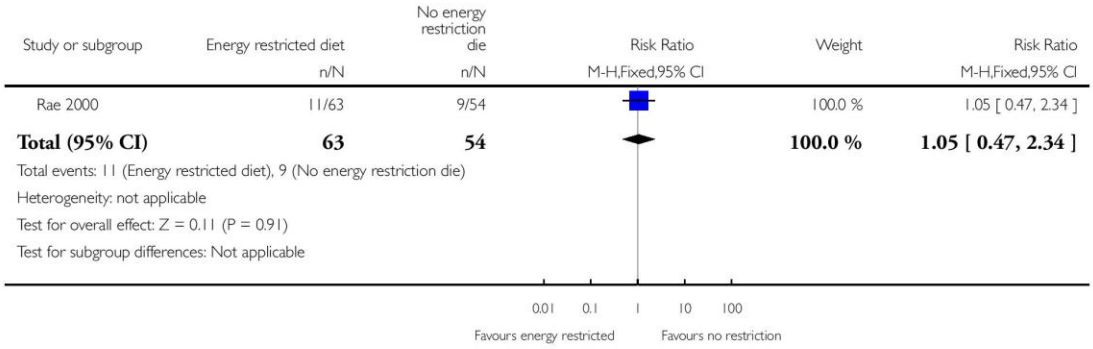


Analysis 3.9. Comparison 3 Energy-restricted diet versus no energy restriction diet, Outcome 9 Insulin or oral hypoglycaemic agent required for hyperglycaemia.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 3 Energy-restricted diet versus no energy restriction diet

Outcome: 9 Insulin or oral hypoglycaemic agent required for hyperglycaemia



Analysis 3.10. Comparison 3 Energy-restricted diet versus no energy restriction diet, Outcome 10 Insulin sensitivity.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 3 Energy-restricted diet versus no energy restriction diet

Outcome: 10 Insulin sensitivity

Study or subgroup	Energy restricted diet N	Mean(SD)	No energy restriction die N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
1 Fasting plasma glucose (mmol)							
Magee 1990	7	4.9 (0.7)	5	5.2 (0.9)		100.0 %	-0.35 [-1.51, 0.81]
Subtotal (95% CI)	**7**		**5**			**100.0 %**	**-0.35 [-1.51, 0.81]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.59 (P = 0.55)							
2 Fasting plasma insulin (pM)							
Magee 1990	7	145 (130)	5	165 (55)		100.0 %	-0.17 [-1.32, 0.98]
Subtotal (95% CI)	**7**		**5**			**100.0 %**	**-0.17 [-1.32, 0.98]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.30 (P = 0.77)							
Test for subgroup differences: Chi^2 = 0.05, df = 1 (P = 0.83), I^2 =0.0%							

Analysis 4.1. Comparison 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 1 Macrosomia (birthweight greater than 4000 g).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 1 Macrosomia (birthweight greater than 4000 g)

Study or subgroup	Low carbohydrate diet n/N	High carbohydrate diet n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Cypryk 2007	0/15	0/15		0.0 [0.0, 0.0]
Total (95% CI)	**15**	**15**		**0.0 [0.0, 0.0]**
Total events: 0 (Low carbohydrate diet), 0 (High carbohydrate diet)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Test for subgroup differences: Not applicable				

Analysis 4.2. Comparison 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 2 Caesarean section.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 2 Caesarean section

Study or subgroup	Low carbohydrate diet n/N	High carbohydrate diet n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Cypryk 2007	7/15	5/15		100.0 %	1.40 [0.57, 3.43]
Total (95% CI)	**15**	**15**		**100.0 %**	**1.40 [0.57, 3.43]**
Total events: 7 (Low carbohydrate diet), 5 (High carbohydrate diet)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.74 (P = 0.46)					
Test for subgroup differences: Not applicable					

Analysis 4.3. Comparison 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 3 Operative vaginal birth.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 3 Operative vaginal birth

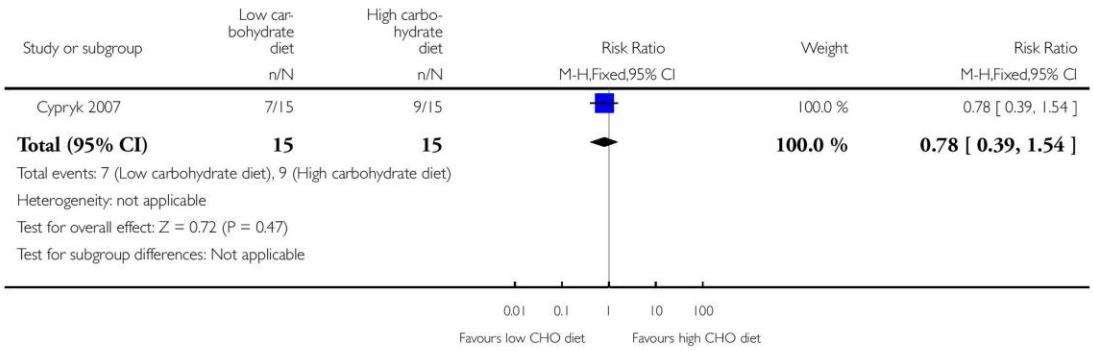
Study or subgroup	Low carbohydrate diet n/N	High carbohydrate diet n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Cypryk 2007	1/15	1/15		100.0 %	1.00 [0.07, 14.55]
Total (95% CI)	**15**	**15**		**100.0 %**	**1.00 [0.07, 14.55]**
Total events: 1 (Low carbohydrate diet), 1 (High carbohydrate diet)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					
Test for subgroup differences: Not applicable					

Analysis 4.4. Comparison 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 4 Normal vaginal birth.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 4 Normal vaginal birth

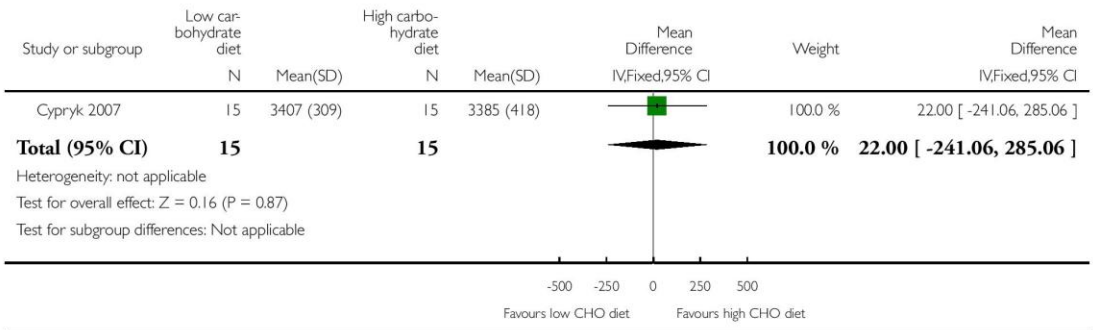


Analysis 4.5. Comparison 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 5 Birthweight (g).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 5 Birthweight (g)

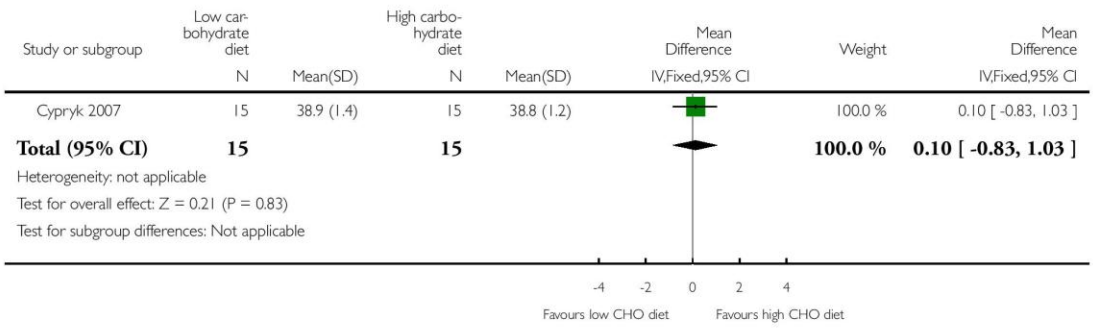


Analysis 4.6. Comparison 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 6 Gestational age at birth (weeks).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 4 Low-carbohydrate (CHO) diet (≤ 45% total energy from CHO) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 6 Gestational age at birth (weeks)

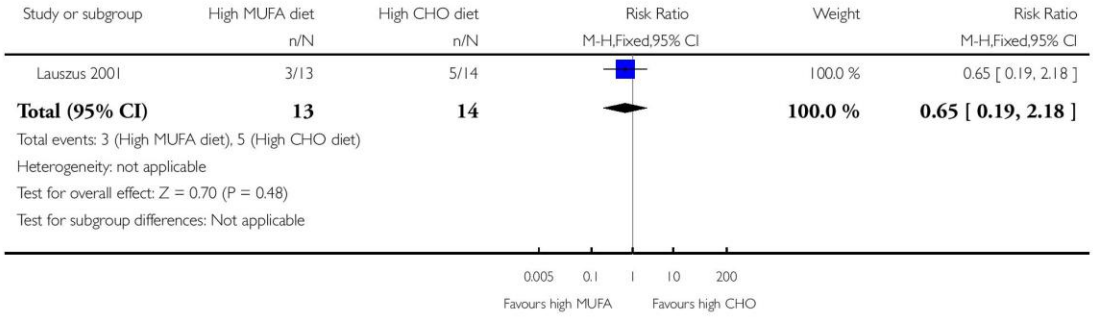


Analysis 5.1. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 1 Macrosomia (birthweight greater than 4000 g).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 1 Macrosomia (birthweight greater than 4000 g)

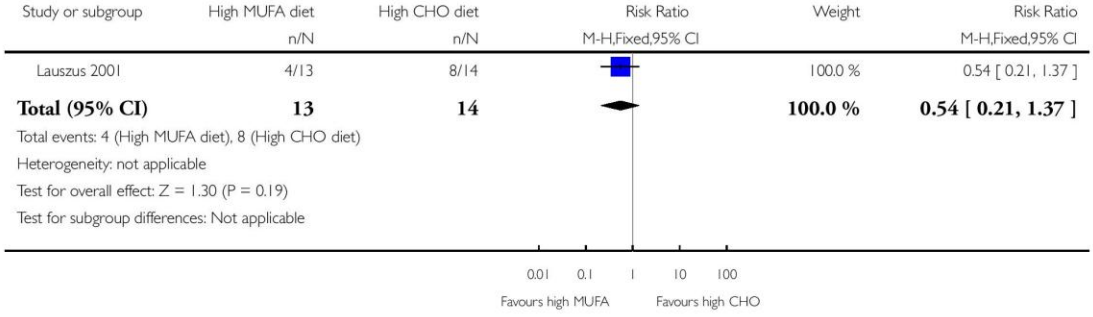


Analysis 5.2. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 2 Large-for-gestational age.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 2 Large-for-gestational age

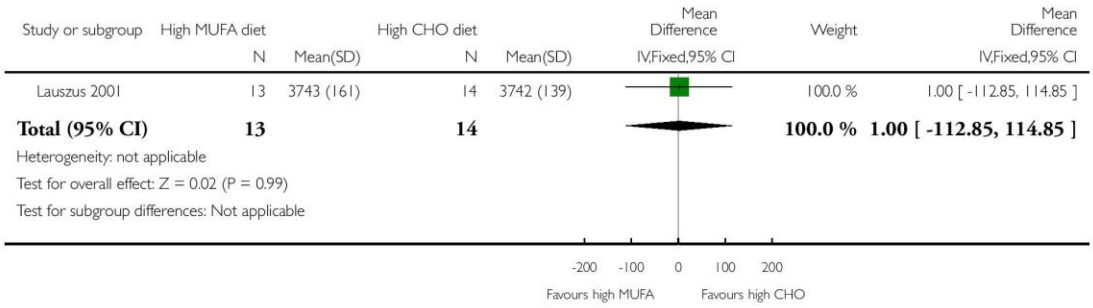


Analysis 5.3. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 3 Birthweight (g).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 3 Birthweight (g)

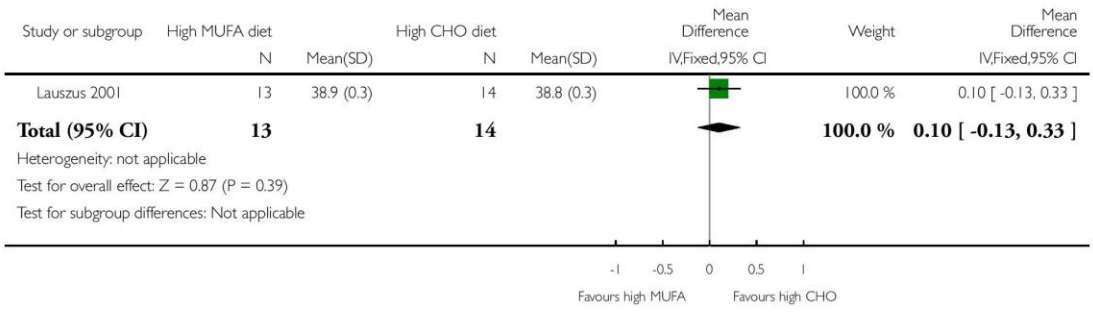


Analysis 5.4. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 4 Gestational age at birth (weeks).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 4 Gestational age at birth (weeks)



Analysis 5.5. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 5 Pre-eclampsia.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 5 Pre-eclampsia

Study or subgroup	High MUFA diet n/N	High CHO diet n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Lauszus 2001	0/13	0/14		0.0 [0.0, 0.0]
Total (95% CI)	**13**	**14**		**0.0 [0.0, 0.0]**
Total events: 0 (High MUFA diet), 0 (High CHO diet)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Test for subgroup differences: Not applicable				

Analysis 5.6. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 6 Insulin or oral hypoglycaemic agent required for hyperglycaemia.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 6 Insulin or oral hypoglycaemic agent required for hyperglycaemia

Study or subgroup	High MUFA diet n/N	High CHO diet n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Lauszus 2001	0/13	0/14		0.0 [0.0, 0.0]
Total (95% CI)	**13**	**14**		**0.0 [0.0, 0.0]**
Total events: 0 (High MUFA diet), 0 (High CHO diet)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Test for subgroup differences: Not applicable				

Analysis 5.7. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 7 Maternal weight at late pregnancy (third trimester) (kg).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 7 Maternal weight at late pregnancy (third trimester) (kg)

Study or subgroup	High MUFA diet N	Mean(SD)	High CHO diet N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Maternal weight at 36 weeks' gestation							
Lauszus 2001	13	100.1 (6.9)	14	87.5 (5.3)		100.0 %	12.60 [7.93, 17.27]
Subtotal (95% CI)	**13**		**14**			**100.0 %**	**12.60 [7.93, 17.27]**
Heterogeneity: not applicable							
Test for overall effect: Z = 5.29 (P < 0.00001)							
2 Maternal weight at 38 weeks' gestation							
Lauszus 2001	13	100.3 (6.6)	14	88.5 (5.4)		100.0 %	11.80 [7.23, 16.37]
Subtotal (95% CI)	**13**		**14**			**100.0 %**	**11.80 [7.23, 16.37]**
Heterogeneity: not applicable							
Test for overall effect: Z = 5.06 (P < 0.00001)							
3 Maternal weight at delivery							
Lauszus 2001	13	100.5 (6.5)	14	88.6 (5.1)		100.0 %	11.90 [7.47, 16.33]
Subtotal (95% CI)	**13**		**14**			**100.0 %**	**11.90 [7.47, 16.33]**
Heterogeneity: not applicable							
Test for overall effect: Z = 5.27 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 0.07, df = 2 (P = 0.97), I^2 =0.0%							

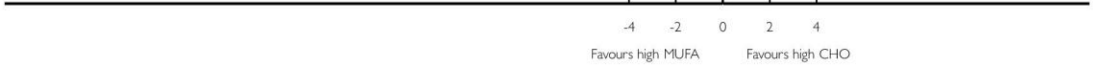
Analysis 5.8. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 8 Maternal BMI at late pregnancy (third trimester) (kg/m2).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 8 Maternal BMI at late pregnancy (third trimester) (kg/m^2)

Study or subgroup	High MUFA diet N	Mean(SD)	High CHO diet N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Maternal BMI at 36 weeks' gestation (kg/m^2)							
Lauszus 2001	13	36.2 (2.4)	14	31.5 (1.5)		100.0 %	4.70 [3.18, 6.22]
Subtotal (95% CI)	**13**		**14**			**100.0 %**	**4.70 [3.18, 6.22]**
Heterogeneity: not applicable							
Test for overall effect: Z = 6.05 (P < 0.00001)							
2 Maternal BMI at 38 weeks' gestation (kg/m^2)							
Lauszus 2001	13	36 (2.4)	14	32.2 (1.7)		100.0 %	3.80 [2.22, 5.38]
Subtotal (95% CI)	**13**		**14**			**100.0 %**	**3.80 [2.22, 5.38]**
Heterogeneity: not applicable							
Test for overall effect: Z = 4.72 (P < 0.00001)							
3 Maternal BMI at delivery (kg/m^2)							
Lauszus 2001	13	36.3 (2.2)	14	32.4 (1.7)		100.0 %	3.90 [2.41, 5.39]
Subtotal (95% CI)	**13**		**14**			**100.0 %**	**3.90 [2.41, 5.39]**
Heterogeneity: not applicable							
Test for overall effect: Z = 5.13 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 0.80, df = 2 (P = 0.67), I^2 =0.0%							



Analysis 5.9. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 9 Maternal postpartum BMI (> 4 months postpartum) (kg/m2).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 9 Maternal postpartum BMI (> 4 months postpartum) (kg/m^2)

Study or subgroup	High MUFA diet N	Mean(SD)	High CHO diet N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Lauszus 2001	13	32.6 (2.8)	14	28.5 (1.7)		100.0 %	4.10 [2.34, 5.86]
Total (95% CI)	**13**		**14**			**100.0 %**	**4.10 [2.34, 5.86]**

Heterogeneity: not applicable

Test for overall effect: Z = 4.56 (P < 0.00001)

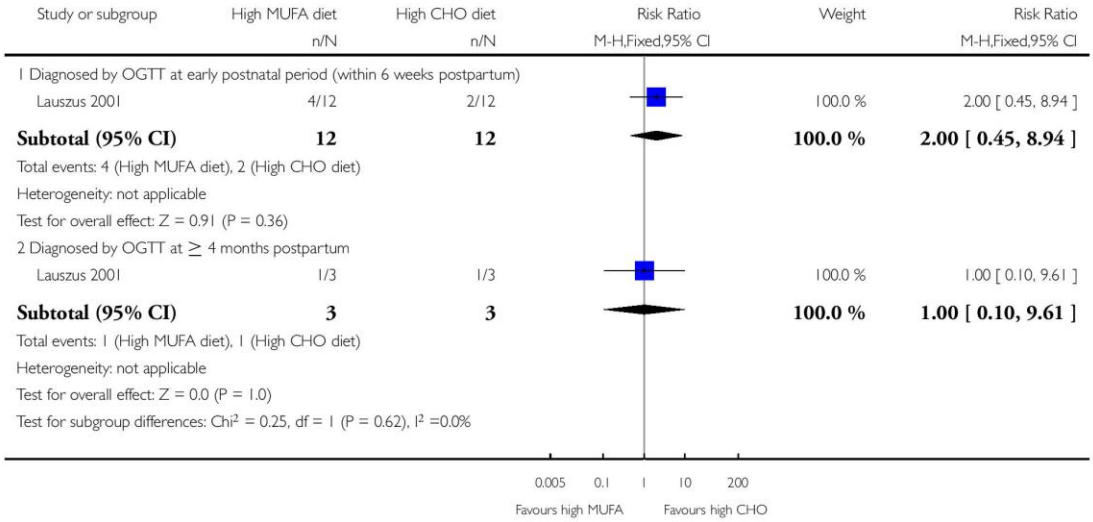
Test for subgroup differences: Not applicable

Analysis 5.10. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 10 Development of type 2 diabetes.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 10 Development of type 2 diabetes

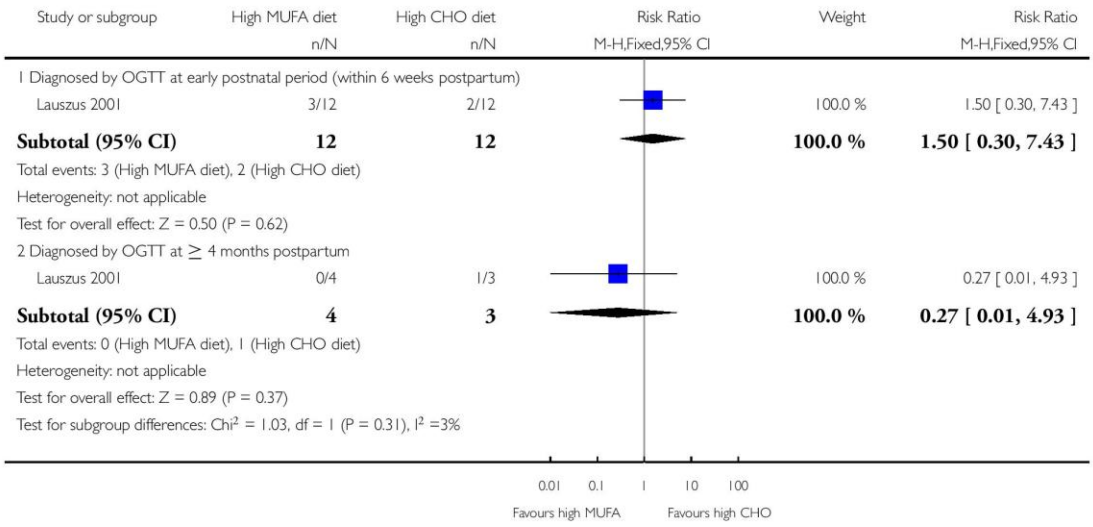


Analysis 5.11. Comparison 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO), Outcome 11 Development of glucose intolerance without meeting type 2 diabetes diagnostic criteria.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 5 High-monounsaturated fat (MUFA) diet (≥ 20% total energy from MUFA) versus high-CHO diet (≥ 50% total energy from CHO)

Outcome: 11 Development of glucose intolerance without meeting type 2 diabetes diagnostic criteria

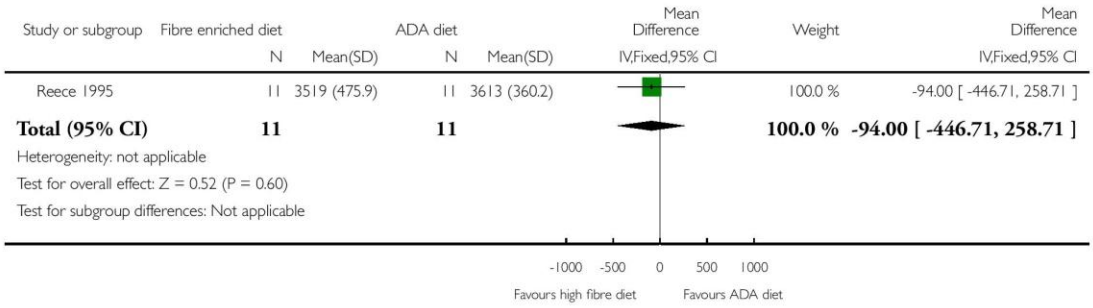


Analysis 6.1. Comparison 6 Standard ADA diet (20 g fibre/day) versus fibre-enriched diet (80 g fibre/ day), Outcome 1 Birthweight (g).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 6 Standard ADA diet (20 g fibre/day) versus fibre-enriched diet (80 g fibre/ day)

Outcome: 1 Birthweight (g)

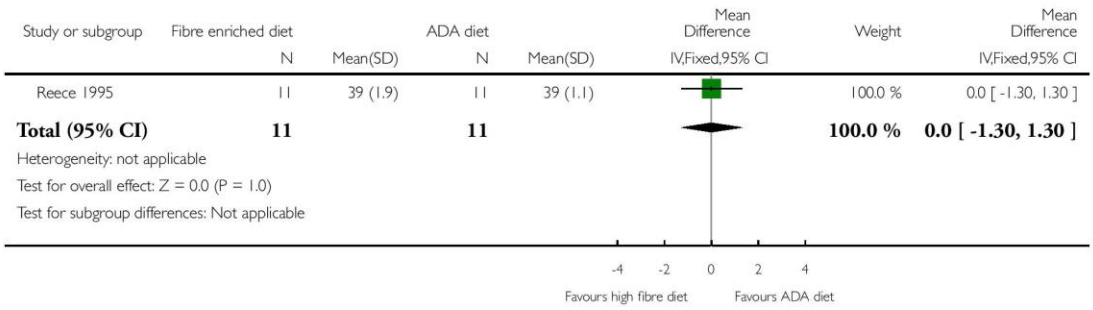


Analysis 6.2. Comparison 6 Standard ADA diet (20 g fibre/day) versus fibre-enriched diet (80 g fibre/ day), Outcome 2 Gestational age at birth (weeks).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 6 Standard ADA diet (20 g fibre/day) versus fibre-enriched diet (80 g fibre/ day)

Outcome: 2 Gestational age at birth (weeks)

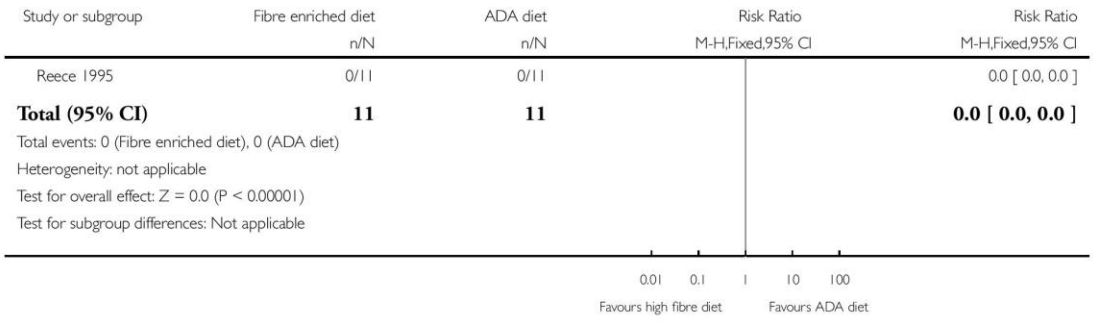


Analysis 6.3. Comparison 6 Standard ADA diet (20 g fibre/day) versus fibre-enriched diet (80 g fibre/ day), Outcome 3 Insulin or oral hypoglycaemic agent required for hyperglycaemia.

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 6 Standard ADA diet (20 g fibre/day) versus fibre-enriched diet (80 g fibre/ day)

Outcome: 3 Insulin or oral hypoglycaemic agent required for hyperglycaemia

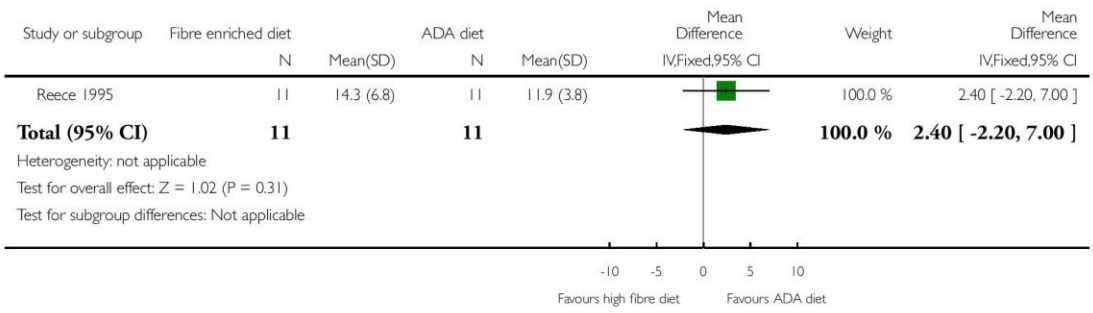


Analysis 6.4. Comparison 6 Standard ADA diet (20 g fibre/day) versus fibre-enriched diet (80 g fibre/ day), Outcome 4 Gestational weight gain (kg).

Review: Different types of dietary advice for women with gestational diabetes mellitus

Comparison: 6 Standard ADA diet (20 g fibre/day) versus fibre-enriched diet (80 g fibre/ day)

Outcome: 4 Gestational weight gain (kg)



APPENDICES

Appendix 1. WOMBAT Perinatal Trials Registry search strategy

We searched trials in the Women and Babies Health and Wellbeing: Action through Trials (WOMBAT) Perinatal Trials Registry using the terms of "gestational diabetes mellitus", "pregnancy", "pregnant", "glucose intolerance", "diet", "dietary advice", "nutrition". We reviewed all relevant trials listed under the search results.

CONTRIBUTIONS OF AUTHORS

Shanshan Han wrote drafts of the protocol and review, with Caroline Crowther and Philippa Middleton contributing to data extraction, and commenting on and editing to all drafts. Emer Heatley was involved in data extraction and assessment of risk of bias of the included studies.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- ARCH, Robinson Institute, The University of Adelaide, Australia.

External sources

- Australian Department of Health and Ageing, Australia.
- NHMRC: National Health and Medical Research Council, Australia.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Maternal secondary outcomes of maternal weight at late pregnancy (third trimester) and maternal BMI at late pregnancy (third trimester) were added.

INDEX TERMS

Medical Subject Headings (MeSH)

Caloric Restriction; Diabetes, Gestational [*diet therapy]; Diabetic Diet; Diet, Carbohydrate-Restricted; Dietary Carbohydrates [administration & dosage]; Dietary Fiber [administration & dosage]; Glycemic Index; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Pregnancy

4 Cochrane systematic review: interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

This chapter includes a published Cochrane systematic review entitled “Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria”. An authorship statement including publication details has been attached on the next page.

4.1

Statement of Authorship

Title of Paper	Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria
Publication Status	◉ Published, ○ Accepted for Publication, ○ Submitted for Publication, ○ Publication style
Publication Details	

Author Contributions

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

Name of Principal Author (Candidate)	Shanshan Han		
Contribution to the Paper	Performed data extraction and assessment of risk of bias of the included studies; performed data analysis and data interpretation; wrote drafts of the protocol and review; acted as corresponding author.		
Signature		Date	31/3/14

Name of Co-Author	Caroline Crowther		
Contribution to the Paper	Contributed to data extraction, assessment of risk of bias of the included studies, data analysis and data interpretation; commented on and edited all drafts; supervised development and the progress of work.		
Signature		Date	19/3/14

Name of Co-Author	Philippa Middleton		
Contribution to the Paper	Performed data extraction and assessment of risk of bias of the included studies;contributed to data analysis and data interpretation; commented on and edited all drafts; supervised development and the progress of work.		
Signature		Date	27/3/14

Name of Co-Author			
Contribution to the Paper			
Signature		Date	

Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria (Review)

Han S, Crowther CA, Middleton P

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2012, Issue 1

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WILEY

TABLE OF CONTENTS

[Intervention Review]

Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

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ABSTRACT

Background

Pregnancy hyperglycaemia without meeting gestational diabetes mellitus (GDM) diagnostic criteria affects a significant proportion of pregnant women each year. It is associated with a range of adverse pregnancy outcomes. Although intensive management for women with GDM has been proven beneficial for women and their babies, there is little known about the effects of treating women with hyperglycaemia who do not meet diagnostic criteria for GDM and type 2 diabetes (T2DM).

Objectives

To assess the effects of different types of management strategies for pregnant women with hyperglycaemia not meeting diagnostic criteria for GDM and T2DM (referred as borderline GDM in this review).

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 September 2011).

Selection criteria

Randomised and cluster-randomised trials comparing alternative management strategies for women with borderline GDM.

Data collection and analysis

Two review authors independently assessed study eligibility, extracted data and assessed risk of bias of included studies. Data were checked for accuracy.

Main results

We included four trials involving 543 women and their babies (but only data from 521 women and their babies is included in our analyses). Three of the four included studies had moderate to high risk of bias and one study was at low to moderate risk of bias. Babies born to women receiving management for borderline GDM (generally dietary counselling and metabolic monitoring) were less likely to be macrosomic (birthweight greater than 4000 g) (three trials, 438 infants, risk ratio (RR) 0.38, 95% confidence interval (CI) 0.19 to 0.74) or large-for-gestational (LGA) age (three trials, 438 infants, RR 0.37, 95% CI 0.20 to 0.66) when compared with those born to women in the routine care group. There were no significant differences in rates of caesarean section (three trials, 509 women, RR 0.93, 95% CI 0.68 to 1.27) and operative vaginal birth (one trial, 83 women, RR 1.37, 95% CI 0.20 to 9.27) between the two groups.

Authors' conclusions

This review found interventions including providing dietary advice and blood glucose level monitoring for women with pregnancy hyperglycaemia not meeting GDM and T2DM diagnostic criteria helped reduce the number of macrosomic and LGA babies without increasing caesarean section and operative vaginal birth rates. It is important to notice that the results of this review were based on four small randomised trials with moderate to high risk of bias without follow-up outcomes for both women and their babies.

PLAIN LANGUAGE SUMMARY

Management of pregnant women with borderline gestational diabetes mellitus

Gestational diabetes mellitus (GDM) is usually said to be any degree of glucose intolerance or high blood glucose level (hyperglycaemia) that is first recognised during pregnancy. Yet no immediately obvious cut-off points can be labelled as abnormal. It is unclear when treatment should be provided to normalise the blood glucose, as the relationship between increased hyperglycaemia and adverse pregnancy outcomes appears to be continuous. Pre-eclampsia in the mother, birthweight greater than 4000 g (macrosomia), birth trauma with large-for-gestational age (LGA) babies, and a future risk of obesity and diabetes in the mothers and babies are all associated with hyperglycaemia during pregnancy. Intensive management involving lifestyle interventions and metabolic monitoring for women with GDM has been proven beneficial for women and their babies.

This review found dietary advice or counselling and blood glucose level monitoring for women with borderline GDM helped reduce the number of macrosomic and LGA babies. A single trial found that the interventions led to more inductions of labour. The interventions did not increase the risk of caesarean sections, operative vaginal births or women's weight gain in pregnancy. These findings were based on four small randomised controlled trials (involving 543 women). The trials were of moderate to high risk of bias and only data from 521 women and their babies is included in our analyses. Until additional evidence from large well designed randomised trials becomes available, current evidence is insufficient to make conclusive recommendations for the management of women with pregnancy high blood glucose concentrations not meeting GDM (or type 2 diabetes) diagnostic criteria.

BACKGROUND

Description of the condition

Introduction and definition of pregnancy hyperglycaemia meeting and without meeting GDM diagnostic criteria

Gestational diabetes mellitus (GDM) is usually defined as 'any degree of glucose intolerance or any severity of hyperglycaemia (high blood glucose level) with onset or first recognition during pregnancy' (Metzger 1998; WHO 1999). Therefore, GDM may include previously undetected type 1 (T1DM) or type 2 (T2DM) diabetes or diabetes presenting only during pregnancy (Metzger 1998).

Screening for GDM is usually by either a universal screening procedure (all pregnant women are screened for GDM) or a selective risk-related procedure (only pregnant women with one or

more risk factors for GDM are screened) (ADA 2009). Regardless of which policy is used for screening, the diagnosis of GDM is usually based on either a 75-gram two-hour oral glucose tolerance test (OGTT) or a 100-gram three-hour OGTT (ADA 2009; Hoffman 1998; IADPSG 2010; NICE 2008; WHO 1999). However, different health bodies recommend slightly different criteria for GDM diagnosis in regard to OGTT, which means different populations of women are labelled as having GDM in different parts of the world (IADPSG 2010). Moreover, the recommendations on GDM diagnostic criteria have changed over time, sometimes due to the changing understanding about the effects of hyperglycaemia on pregnancy outcomes (Coustan 2010).

Some women have glucose concentrations that do not meet diagnostic criteria for GDM, but which are toward the upper end of the recommended normal range. As for women with GDM, these women are at increased risk of adverse pregnancy outcomes. Interventions lowering blood glucose concentrations may be beneficial for them.

Aetiology of pregnancy hyperglycaemia

Insulin, secreted by pancreatic beta cells in response to increasing blood glucose concentrations, helps to maintain normal concentrations. Either inadequate insulin secretion (such as in T1DM) or insulin resistance (defined as insulin acting less effectively in promoting glucose uptake) (such as in T2DM or GDM) can result in hyperglycaemia.

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

Epidemiology of pregnancy hyperglycaemia

The prevalence of GDM is rising worldwide with 1% to 14% of pregnancies being affected (Bottalico 2007; Dabelea 2005; Ferrara 2007; Ragnarsdottir 2010). In low-risk populations, the estimated GDM prevalence is 1.4% to 2.8% (Mulla 2010); in higher risk populations, the estimated prevalence is 3.3% to 6.1% and in some high-risk populations, the prevalence may be higher than 10% (Mulla 2010).

Few data are available on the prevalence of pregnancy hyperglycaemia which does not meet GDM diagnostic criteria. Data from Australian studies suggest that in addition to the 5.5% to 8.8% women with GDM, a further 7% of all pregnant women have hyperglycaemia not meeting GDM diagnostic criteria each year (normal 75-gram OGTT was defined as fasting blood glucose less than 5.5 mmol/L, and two-hour blood glucose less than 7.8 mmol/L) (Dodd 2007; Ju 2008). Results from a US study indicated the prevalence of pregnancy hyperglycaemia without meeting GDM diagnostic criteria was about 8.8% (normal 100-gram OGTT was defined as fasting glucose less than 5.6 mmol/L (100 mg/dL); one-hour glucose less than 10.6 mmol/L (190 mg/dL); two-hour glucose less than 9.2 (165 mg/dL); three-hour glucose less than 8.1 (145 mg/dL) (Stamilio 2004).

Risk factors for pregnancy hyperglycaemia

There are a range of known risk factors for hyperglycaemic disorders during pregnancy. Advanced maternal age and maternal overweight/obesity are among the most common risk factors (Morisset 2010). Women with some specific ethnicities are at higher risk of developing pregnancy hyperglycaemia; these include African-American, Asian-American, Native American, African, Hispanic, Asian, Pacific Islander, and Indigenous Australian (ADA 2009; Ben-Haroush 2004; Hoffman 1998; Petry 2010). Other risk factors include: history of having a macrosomic (birthweight 4000 g or more) infant, history of GDM, family history of diabetes mellitus, maternal high or low birthweight, high parity, polycystic ovarian syndrome and cigarette smoking (Cypryk 2008; Petry 2010; Solomon 1997). Diet and lifestyle factors, such as low fibre and high glycaemic load diet and physical inactivity, are also associated with an increased risk of pregnancy hyperglycaemia (Chasan-Taber 2008; Zhang 2006).

Clinical outcomes for women with pregnancy hyperglycaemia

Pregnancy hyperglycaemia affects both mothers and their babies. The effects of maternal hyperglycaemia on the pregnancy outcomes do not occur at specific thresholds but are increased on a continuum with increasing hyperglycaemia (Metzger 2008).

1) Maternal outcomes related to pregnancy hyperglycaemia

For women with pregnancy hyperglycaemia, there is an increased risk of developing pre-eclampsia and an increased use of induction of labour (Anderberg 2010; Crowther 2005; Dodd 2007; Ju 2008; Landon 2009; Metzger 2008; Sermer 1998). The risk of having caesarean section is also increased (Dodd 2007; Landon 2009; Metzger 2008; Sermer 1998). Due to the risk of having a large-for-gestational-age (LGA) or macrosomic baby, mothers are at higher risk of cephalopelvic disproportion, uterine rupture, shoulder dystocia and perineal lacerations (Jastrow 2010). Evidence from a systematic review showed hyperglycaemia in pregnancy was highly predictive for the later development of diabetes, with more than 50% of women with GDM developing type 2 diabetes mellitus within 10 years of the index pregnancy (Kim 2002).

There are a range of known health risks associated with pregnancy hyperglycaemia without meeting GDM diagnostic criteria. A large multicentre and multiethnic cohort study (HAPO study) of 25,505 women assessed the effect of maternal hyperglycaemia on pregnancy outcomes (Metzger 2008). This study found a significant, continuous association between maternal glucose concentrations below those for a diagnosis of GDM and caesarean section and pre-eclampsia (Metzger 2008). Similarly, data from 16,975 women who gave birth at a tertiary Australian hospital from 1993 to 2003 showed that women with borderline GDM had increased risk of pre-eclampsia and caesarean section, and their infants were at increased risk of hypoglycaemia and hyperbilirubinaemia compared with women having normal glucose tolerance and their babies (Dodd 2007). Borderline GDM was defined as a positive OGCT (blood glucose 7.8 mmol/L or more; one hour after a 50 g glucose load) and a normal 75 g OGTT (fasting blood glucose less than 5.5 mmol/L and two-hour blood glucose less than 7.8 mmol/L) (Dodd 2007). Another Australian study that recruited 1804 primiparous women from four different states assessed the effect of borderline GDM (blood glucose 7.8 mmol/L or more one hour after a 50 g glucose load) and a normal 75 g OGTT (fasting blood glucose less than 5.5 mmol/L and two-hour blood glucose less than 7.8 mmol/L) on pregnancy outcomes (Ju 2008). Women with borderline GDM were at increased risk of a serious maternal outcome, pregnancy hypertension and caesarean section (Ju 2008).

2) Neonatal, infant and later outcomes related to pregnancy hyperglycaemia

Any degree of maternal hyperglycaemia, whether meeting GDM diagnostic criteria or not, exposes the fetus to an intrauterine environment of increased concentrations of glucose through transplacental passage (Reece 2009). As maternal insulin does not cross the placenta from the mother to fetus, the fetus is forced to increase its own insulin secretion (Reece 2009). Excessive insulin produced by the fetus may lead to fetal over-growth, known as LGA; or a birthweight of 4000 g or more (Ju 2008; Metzger 2008; Reece 2009). Birthweight of 4000 g or more, known as macrosomia, complicates about 50% of pregnancies with GDM, which includes women with optimal glycaemic control through interventions (Catalano 2003). Moreover, babies born to women with pregnancy hyperglycaemia have significantly greater skinfold measures and fat mass compared with infants of women with normal glucose tolerance (Catalano 2003; McFarland 1998; Vohr 1997). Being a LGA fetus or macrosomic infant is a surrogate for many of the complications associated with pregnancy hyperglycaemia (Esakoff 2009; Metzger 2008). Babies who are LGA or macrosomic are at increased risk of injury during birth, such as shoulder dystocia, perinatal asphyxia, bone fractures and nerve palsies (Henriksen 2008; Langer 2005; Metzger 2008).

After birth, babies of women with hyperglycaemic disorders are at higher risk of having other neonatal complications such as respiratory distress syndrome, hypoglycaemia, hyperbilirubinaemia (increased levels of bilirubin in the blood), cardiomyopathy (the deterioration of the function of the myocardium), hypocalcaemia, hypomagnesaemia, polycythaemia, hyperviscosity and admission to neonatal nursery (Ju 2008; Metzger 2008; Reece 2009; Soler 1978).

In the longer term, children born to mothers with hyperglycaemia are at increased risk of being overweight or obese in childhood and adulthood regardless of their birthweight, developing T1DM and T2DM and having impaired intellectual achievement (Harder 2009; Mulla 2010; Petitt 1985; Rizzo 1997; Whincup 2008; Yogev 2009).

At every age measured, the offspring of women with GDM are heavier (adjusted for height) and higher adiposity than the offspring of women with normal glycaemia during pregnancy (Pettitt 1983; Petitt 1985; Vohr 1997; Vohr 1999). In addition, there is a positive trend for increasing childhood obesity at age of five to seven years across the range of increasing maternal hyperglycaemia during pregnancy, which remained after adjustment for maternal weight gain, maternal age, parity, ethnicity and birthweight (Hillier 2007).

Infants born LGA are also at increased risk of developing the metabolic syndrome (a cluster of risk factors defined by the occurrence of three of the following: obesity, hypertension, hypertriglyceridaemia and low high-density lipoprotein cholesterol concentration) in childhood, adolescence and adulthood (Barker 1994; Guerrero-Romero 2010; Harder 2009). Childhood development of the metabolic syndrome predicts adult T2DM at 25 to 30 years of age (Morrison 2008). These health problems continue across generations (Mulla 2010; Petitt 1985). Evidence also shows LGA and macrosomia may be associated with increased risk of developmental delay (Ornoy 2005; Rizzo 1997; Slining 2010) and premenopausal breast cancer (Forman 2005).

Description of the intervention

Treatment for pregnancy hyperglycaemia

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

Providing dietary and exercise advice is usually recommended as the primary therapeutic strategy for women with GDM to achieve acceptable glycaemic control (ACOG 2001; Hoffman 1998; NICE 2008). Evidence from randomised controlled trials

had suggested that diet and exercise interventions were effective in improving pregnancy outcomes for women with pregnancy hyperglycaemia (Bonomo 2005; Crowther 2005; Landon 2009).
If these interventions alone are not enough to achieve good maternal glycaemic control, insulin therapy may be indicated (ACOG 2001; Hoffman 1998; NICE 2008). Oral hypoglycaemics such as glyburide and metformin have been used as alternatives to insulin therapy (Alwan 2009; Silva 2010; Simmons 2004). As a part of management for GDM, maternal glucose monitoring is always used for guiding treatment and ultrasonography helps to guide management of birth (ACOG 2001; Hoffman 1998).
A Cochrane review assessed the effect of these management interventions for women with GDM on maternal and infant outcomes (Alwan 2009), and found such management was effective and beneficial for women with GDM and their infants (Alwan 2009). Similar findings were reported in another systematic review on the effects of treatment in women with GDM (Horvath 2010). What is uncertain is whether these interventions are beneficial for women with a lower degree of pregnancy hyperglycaemia (Landon 2010; Sacks 2009).

Why it is important to do this review

Pregnancy hyperglycaemia without meeting GDM diagnostic criteria affects a significant proportion of pregnant women (Dodd 2007; Ju 2008; Rumbold 2006; Stamilio 2004). Hyperglycaemia during pregnancy is associated with adverse pregnancy outcomes including macrosomia, respiratory distress syndrome and future development of obesity and T1DM or T2DM in the offspring (Dabelea 2000; Dabelea 2007; Harder 2009; Hillier 2007; Metzger 2008; Silverman 1995) and pre-eclampsia, birth trauma, and development of type 2 diabetes in the mother (Kim 2002; Metzger 2008). The relationship between increased hyperglycaemia and the adverse pregnancy outcomes appears to be continuous (Metzger 2008; Mulla 2010). There are no immediately obvious cut-off points which can be labelled as abnormal to diagnose GDM (Metzger 2008; Mulla 2010). It is therefore unclear at what degree of pregnancy hyperglycaemia 'treatment' should be provided to normalise blood glucose.
Although intensive management of GDM has been proven beneficial for women with GDM and their babies (Alwan 2009; Crowther 2005; Horvath 2010; Landon 2009), there is little known about the effects of managing women with hyperglycaemia who do not meet diagnostic criteria for GDM and T2DM. This review aims to provide reliable evidence to guide the best care for women with pregnancy hyperglycaemia not meeting GDM diagnostic criteria.

OBJECTIVES

To assess the effects of different types of management strategies for pregnant women with hyperglycaemia not meeting diagnostic criteria for gestational diabetes mellitus (GDM) and type 2 diabetes (referred to as borderline GDM in this review).

METHODS

Criteria for considering studies for this review

Types of studies

All published randomised controlled trials (RCTs) and cluster-randomised trials comparing alternative management strategies for women with borderline gestational diabetes mellitus (GDM). We intended to include published abstracts for RCTs and cluster-RCTs if relevant outcome data were available. We planned to exclude quasi-RCTs and crossover trials.

Types of participants

Pregnant women with hyperglycaemia who do not meet the diagnostic criteria for GDM. Diagnostic criteria for GDM based on oral glucose tolerance test results are defined variously by individual trialists according to local health authorities and professional organisations.
Women were eligible regardless of gestation, age, parity or plurality. Women with pre-existing diabetes mellitus and previously treated GDM were not eligible.
We intended to included trials that included pregnant women with normal glycaemia, GDM or pre-existing diabetes mellitus if we could extract subgroup data for women with hyperglycaemia not meeting diagnostic criteria separately.

Types of interventions

We planned to include any form of management for women with pregnancy hyperglycaemia not meeting GDM diagnostic criteria above routine antenatal care in the review. These included any type of dietary advice (standard or individualised), exercise and lifestyle advice (standard or individualised) and drug treatment including insulin and oral drugs.
One type of intervention compared with standard antenatal care. These included: any type of dietary advice (standard or individualised) compared with standard antenatal care; any type of exercise advice (standard or individualised) compared with standard antenatal care; drug treatment compared with standard antenatal care. Multiple forms of intervention compared with standard care, i.e. diet and exercise advice compared with standard antenatal care;

diet and exercise advice and drug treatment compared with standard antenatal care. Two forms of management would be compared against each other, i.e. diet and exercise advice compared with drug treatment. Two or more types of the same form of management could be compared against each other, i.e. standard dietary advice compared with individualised dietary advice; standard exercise advice compared with individualised exercise advice; different types of dietary advice could be compared with each other; insulin treatment could be compared with oral drug treatment.

Types of outcome measures

Primary outcomes

Fetal/neonatal outcomes

1. Fetal/neonatal mortality;
2. LGA (birthweight greater than or equal to 90th percentile for gestational age);
3. macrosomia (birthweight greater than 4000 g or greater than 4500 g as defined by authors).

Maternal outcomes

1. Mode of birth (normal vaginal birth, operative vaginal birth, caesarean section).

Secondary outcomes

Fetal/neonatal outcomes

1. Neonatal hypoglycaemia requiring treatment (variously defined by authors of individual trials);
2. gestational age at birth;
3. preterm birth (less than 37 weeks' gestation);
4. birthweight;
5. small-for-gestational age;
6. shoulder dystocia;
7. bone fracture;
8. nerve palsy;
9. respiratory distress syndrome;
10. use of assisted ventilation;
11. hyperbilirubinaemia requiring treatment;
12. Apgar scores (less than seven at five minutes);
13. Apgar scores (less than four at five minutes);
14. Ponderal index*;
15. skinfold thickness measurements.

* a measure of leanness of a person calculated as a relationship between mass and height; can provide valid results even for very short and very tall persons.

Childhood outcomes

1. Weight;
2. height;
3. body mass index (BMI);
4. fat mass/fat-free mass;
5. skinfold thickness measurements;
6. blood pressure;
7. impaired glucose tolerance (as defined by author(s));
8. type 1 diabetes;
9. type 2 diabetes;
10. insulin sensitivity (as defined by author(s));
11. dyslipidaemia or metabolic syndrome;
12. childhood neurodisability;
13. educational achievement.

Adulthood

1. Weight;
2. height;
3. BMI;
4. fat mass/fat-free mass;
5. skinfold thickness measurements;
6. blood pressure;
7. impaired glucose tolerance (as defined by author(s));
8. development of type 1 diabetes;
9. development of type 2 diabetes;
10. insulin sensitivity (as defined by author(s));
11. dyslipidaemia or metabolic syndrome;
12. educational achievement.

Maternal outcomes

Perinatal

1. Pre-eclampsia;
2. insulin or oral hypoglycaemic agent required for hyperglycaemia;
3. weight gain during pregnancy (according to IOM 2009 pregnancy weight gain guidelines);
4. induction of labour;
5. augmentation of labour;
6. perineal trauma;
7. postpartum haemorrhage;
8. postpartum infection;
9. adherence to treatment;
10. women's sense of well-being and quality of life (as defined by author(s));
11. women's view of intervention.

Long term

1. Postnatal weight retention;
2. BMI;
3. gestational diabetes in subsequent pregnancy;
4. development of type 2 diabetes mellitus;
5. development of type 1 diabetes mellitus;
6. impaired glucose tolerance (as defined by author(s));
7. insulin sensitivity (as defined by author(s)).

Health services cost

1. Number of hospital visits/antenatal visits for mother;
2. dietitian visits;
3. medical physician visits;
4. cost for blood glucose monitoring during pregnancy;
5. costs to families in relation to the management provided;
6. length of postnatal stay (mother);
7. admission to neonatal nursery/neonatal intensive care unit;
8. length of postnatal stay (baby);
9. cost of maternal care;
10. cost of offspring care.

Search methods for identification of studies

Electronic searches

We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (30 September 2011).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

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

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

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Two review authors independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We resolved disagreements through discussion and consulted a third author as necessary.

Data extraction and management

We designed a form to extract data. For eligible studies, at least two review authors extracted the data using the agreed form. We resolved discrepancies through discussion. We entered data into Review Manager software (RevMan 2011) and checked for accuracy.

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias for each 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 assessor.

(1) Sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We 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); or
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal the allocation sequence and determine whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We 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 each 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 each included study the methods used, if any, 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 through withdrawals, dropouts, protocol deviations)

We described for each 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, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we re-included 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 bias

We described for each 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 was clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review had been reported);
- high risk of bias (where not all the study's pre-specified outcomes had been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest were reported incompletely and so could not 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 sources of bias

We described for each included study any important concerns we had about other possible sources of bias.

We assessed whether each 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.

(7) Overall risk of bias

We made explicit judgements about whether studies were 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 we considered it was likely to impact on the findings. We planned to explore the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

Measures of treatment effect

Dichotomous data

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

Continuous data

For continuous data, we used the mean difference if outcomes were measured in the same way between trials. We used the standardised mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials

We did not identify any cluster-randomised trials for inclusion. However, if we identify cluster-randomised trial in future updates

of this review, we will include them in the analyses along with individually randomised trials. We will adjust their sample sizes using the methods described in the *Handbook* using an estimate of the intracluster 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. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely.
We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Dealing with missing data

For included studies, we noted levels of attrition. We explored the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis. For all outcomes, we 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 will be analysed in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial would be the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the T^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if I^2 was greater than 30% and either T^2 was greater than zero, or there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

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

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2011). We used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar. If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary if an average treatment effect across trials was considered clinically meaningful. We treated the random-effects summary as the average range of possible treatment effects and we discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful we would not combine trials.
When we used random-effects analyses, we have presented the results as the average treatment effect with its 95% confidence interval, and the estimates of T^2 and I^2.

Subgroup analysis and investigation of heterogeneity

If we identified substantial heterogeneity, we would have investigated it using subgroup analyses and sensitivity analyses. We planned to consider whether an overall summary was meaningful, and if it was, use random-effects analysis to produce it.
Different types of treatment, ways of delivering treatment, variations in the severity of hyperglycaemia and maternal characteristics may have significant effects on pregnancy outcomes. We planned to carry out the following subgroup analyses, but there were not enough trials included to conduct these subgroup analyses.

1. Maternal characteristics

- Maternal age
  - 35 years of age or more compared with below 35 years of age.
- Maternal body mass index (BMI) at or before trial entry
  - BMI ranges of 18.5 to 24.9 kg/m² compared with less than 18.5 kg/m²;
  - BMI ranges of 18.5 to 24.9 kg/m² compared with 25 to 29.9 kg/m²;
  - BMI ranges of 18.5 to 24.9 kg/m² compared with 30 kg/m² to 39.9 kg/m²;
  - BMI ranges of 18.5 to 24.9 kg/m² compared with 40 kg/m² or more.
- Ethnicity
  - High-risk ethnic group compared with low risk ethnic group.
- Parity

- Parity of 0 compared with 1-2;
- parity of 0 compared with 3 or more.

2. Severity of hyperglycaemia at OGTT diagnostic testing (diagnostic criteria are defined variously by individual trials)

- All blood glucose values below diagnostic cut-off points for GDM compared with one or more values above cut-off points in diagnostic testing;
- one blood glucose value above diagnostic cut-off points for GDM compared with two values above cut-off points in diagnostic testing.

3. Types of treatment

- Dietary advice (standard dietary advice compared with individualised dietary advice);
- exercise/lifestyle intervention (standard exercise/lifestyle intervention compared with individualised exercise/lifestyle intervention);
- oral hypoglycaemics compared with insulin;
- different types of hypoglycaemics (one type of hypoglycaemics compared with another);
- different insulin regimens (one insulin regimen compared with another regimen);
- one form of treatment (e.g. dietary advice alone) compared with multiple forms of treatment (e.g. dietary and exercise advice).

4. Ways of delivering treatment

- Group intervention compared with individual intervention;
- face-to-face intervention compared with non-face-to-face intervention (e.g. phone counselling, information package, etc.).

We planned to use primary outcomes in subgroup analyses.
We planned to assess differences between subgroups by interaction tests where possible.

Sensitivity analysis

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

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search

We identified a total of 35 trials through the search of the PCG Trials Register. Following application of eligibility criteria, 24 trials were not relevant to this review due to the different study population (e.g. women with gestational diabetes mellitus (GDM), or women with normal pregnancy). We included four trials (Bevier 1999; Bonomo 2005; Grant 2011; Langer 1989) and excluded seven trials (Bung 1993; Dunne 2001; Ford 1997; Li 1987; Li 1999; Maresh 1983; Yang 2003). One trial was ongoing (Crowther 2007) and we will consider it for inclusion in the next update. We identified another ongoing trial through contacting one of the trial investigators (Wolever 2011 [pers comm]); we will also consider it for inclusion in next update. *See* Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Included studies

We have included four trials (involving 543 women) in this review (Bevier 1999; Bonomo 2005; Grant 2011; Langer 1989) but data from only 521 women and their babies is included in our analyses Two of the four included studies were from the United States (Bevier 1999; Langer 1989) and one each was from Canada (Grant 2011) and Italy (Bonomo 2005).

Participants

We have included a total of 543 women in this review, and included 521 women in the data analysis. The majority of women (94%) in Bevier 1999's study were white or of Hispanic ethnicity. One-third of women were black, Hispanic or white in Langer 1989's study. Bonomo 2005 included only Caucasian women. Women in Grant 2011's study were from diverse ethnicities of south east Asian, Indian, Caucasian, east Asian, Caribbean, mixed and Hispanic.
Bevier 1999 and Bonomo 2005 included women with a positive 50-gram one-hour GCT but a normal 100-gram three-hour OGTT. Langer 1989 included women with a positive GCT and only one abnormal value on their 100-gram three-hour OGTT. Grant 2011 included women with a positive GCT and only one abnormal value on 75-gram two-hour OGTT.
The National Diabetes Data Group GDM diagnostic criteria were used in Bevier 1999 and Langer 1989. Bonomo 2005 used Carpenter and Coustan's criteria and Grant 2011 used Canadian Diabetes Association (CDA) criteria (details are included in Characteristics of included studies).

Intervention and comparison

Bevier 1999 compared dietary counselling, home glucose monitoring and clinic random glucose check, weekly home glucose monitoring diary review with clinic random blood glucose check only. Insulin therapy was considered for women in both groups in Bevier 1999. In Bonomo 2005, interventions included dietary counselling with follow-ups to assess compliance, fortnightly checking of two-hour postprandial blood glucose, HbA_{1c} and fructosamine at clinic, and daily urine test for ketone bodies at home; women in the control group followed standard care with no diet or pharmacological treatment (Bonomo 2005). All participants in Grant 2011's study received diet counselling, but women in the intervention group were asked to select their starch choices from an exchange list of low glycaemic index (GI) foods, while women in the control group were asked to select their starch choices from an exchange list of intermediate- and high-GI foods, which reflected the typical dietary intake of the local population.

In Langer 1989, interventions included capillary blood glucose monitoring seven times a day, diet counselling and insulin therapy when diet alone was not able to achieve the blood glucose target of 95 mg/dl (5.3 mmol/L); women in the control group received routine diet with baseline capillary blood glucose monitoring for four weeks (Langer 1989).

Outcome

All the four included studies focused on perinatal health related outcomes for women and their babies (Bevier 1999; Bonomo 2005; Grant 2011 Langer 1989). None of the included studies included longer term outcomes for mothers and their babies.

See the Characteristics of included studies table for more details.

Excluded studies

We excluded three trials which were not randomised controlled trials (Li 1987; Li 1999; Maresh 1983). Two trials included women with pregnancy hyperglycaemia who had reached the diagnostic criteria for GDM (Ford 1997; Yang 2003). One trial used fasting plasma glucose values for pregnancy hyperglycaemia diagnosis instead of using OGTT, which did not meet the inclusion criteria for this review (Bung 1993). We excluded one trial as there were no published or unpublished data available (Dunne 2001).

Risk of bias in included studies

Three of the four included studies were at moderate to high risk of bias and one study (Grant 2011) was at low to moderate risk of bias. See Figure 1 and Figure 2.

Figure 1. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

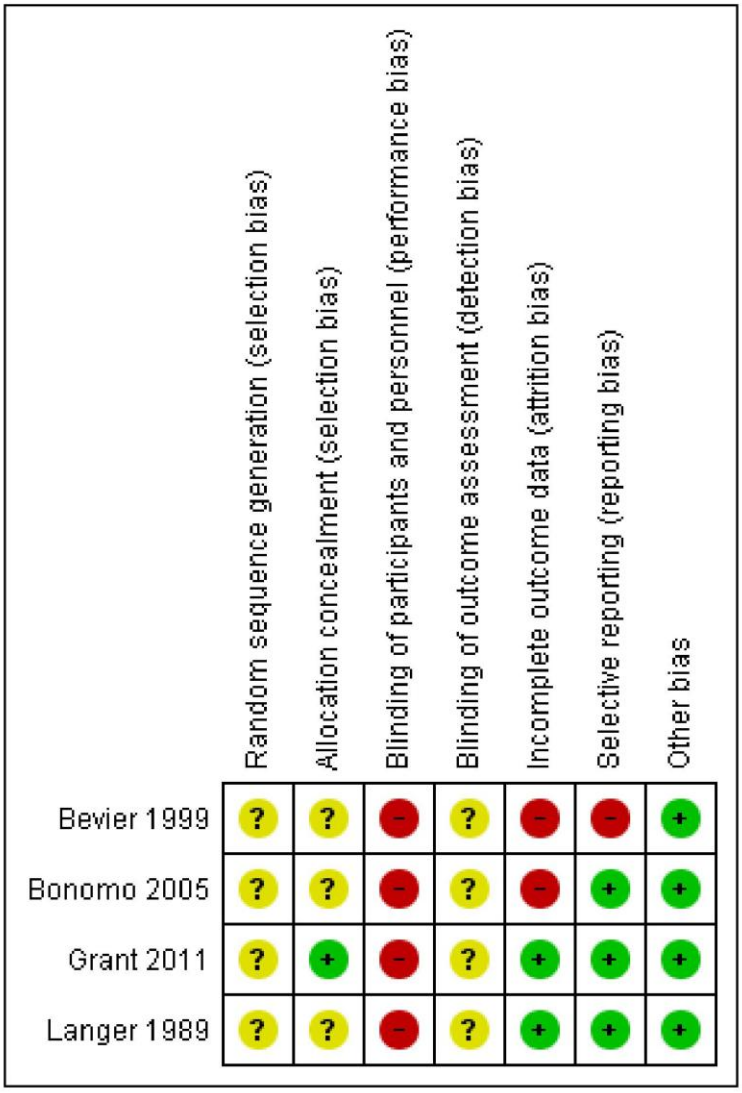
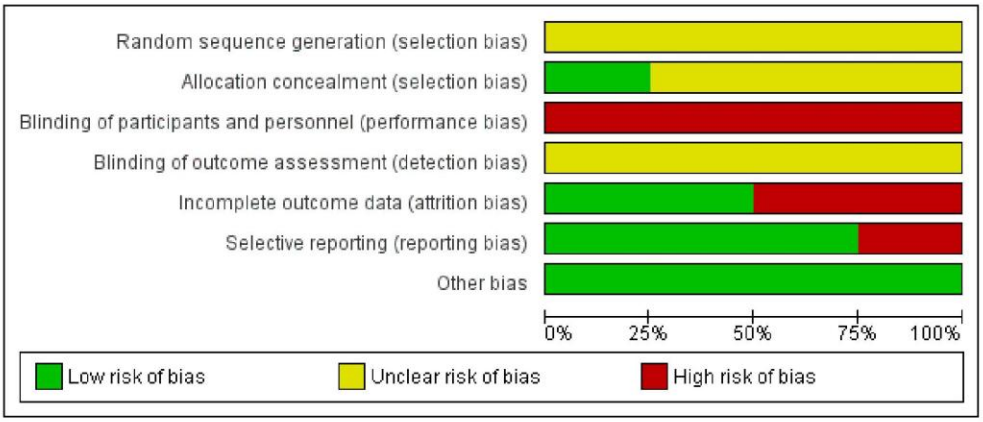


Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

Three trials reported that women were randomly allocated to intervention and control groups, without information on the method of randomisation and allocation concealment (Bevier 1999; Bonomo 2005; Langer 1989). One trial (Grant 2011) used numbered, sealed, opaque envelopes to allocate women to groups, and blocks were used in sequence generation; the randomisation order in this study was generated by one of the investigators who was not involved in recruitment.

Blinding

Grant 2011 described the trial as an "open-label" pilot study. Bonomo 2005 reported that all women and the attending physicians were informed of the results of the GCT and OGTT. Women in this trial were unlikely to be blinded; however, it was unclear about whether research personnel were blinded or not. No information on whether research personnel were blinded or not in Bevier 1999 and Langer 1989; and it is unlikely that participants were blinded in these two trials.

None of the trials reported on whether outcome assessors were blinded (Bevier 1999; Bonomo 2005; Grant 2011; Langer 1989).

Incomplete outcome data

A total of 20 women (19.4%) were excluded post randomisation in Bevier 1999's study. Five women (four in control group, one in experimental group) were excluded due to requiring insulin treatment; another 14 women were excluded due to poor compliance for diet and home blood glucose monitoring (HBGM) in the intervention group or receiving diet counselling and/or HBGM instruction in the control group; one woman was excluded due to therapeutic abortion (Bevier 1999).

In Bonomo 2005, there were six women (2%) in the intervention group lost to follow-up, and nine women (3%) in the intervention group and six (2%) in the control group were excluded post-randomisation due to a diagnosis of GDM during re-evaluation at 30 to 34 weeks' gestation (Bonomo 2005).

There were no losses to follow-up or post-randomisation exclusions reported in Grant 2011 and Langer 1989.

Selective reporting

In Bevier 1999, macrosomia was not clearly defined and the rate of macrosomia was unclear. There was no obvious risk of selective reporting in Bonomo 2005, Grant 2011 and Langer 1989.

Other potential sources of bias

No obvious risk of other potential sources of bias for the included studies was apparent (Bevier 1999; Bonomo 2005; Grant 2011; Langer 1989).

Effects of interventions

Intensive management versus routine care

Primary outcomes

Fetal or neonatal mortality was not reported in Bevier 1999, Bonomo 2005 or Langer 1989. Grant 2011 reported that there were no fetal or neonatal deaths.

Macrosomia and LGA were reported as outcomes in all four included trials. Babies born to women in the intervention group were less likely to be LGA (three trials, 438 infants, risk ratio (RR) 0.37, 95% confidence intervals (CI) 0.20 to 0.66) (Analysis 1.1) or macrosomic (three trials, 438 infants, RR 0.38, 95% CI 0.19 to 0.74) (Analysis 1.2) when compared with those born to women in the routine care group. The overall results gave the number needed to treat of 12 (95% CI 9 to 28) for macrosomia and 10 (95% CI 7 to 17) for LGA. One trial reported results for a combined outcome of LGA or macrosomia (Bevier 1999), which suggested a significantly lower incidence of either LGA or macrosomia in the intervention group when compared with routine care group (one trial, 83 infants, RR 0.11, 95% CI 0.02 to 0.84) (Analysis 1.3).

Macrosomia was defined as birthweight at least 4000 g in Bonomo 2005 and Grant 2011. Langer 1989 reported 82% of the LGA babies were macrosomic, but the definition of macrosomia was not stated in the published paper. LGA was defined as birthweight $\geq 90^{th}$ percentile in Bonomo 2005 and Langer 1989; Grant 2011 defined LGA as more than 90th percentile for sex and gestational age. In Bevier 1999, macrosomia and LGA were not clearly defined, and the results were reported as a combination of macrosomia and LGA.

For maternal primary outcomes, there were no significant differences between treatment groups in rates of caesarean section (three trials, 509 women, RR 0.93, 95% CI 0.68 to 1.27) (Analysis 1.4) or operative vaginal birth (one trial, 83 women, RR 1.37, 95% CI 0.20 to 9.27) (Analysis 1.5).

Secondary outcomes

Babies born to women in the intervention group had slightly, but statistically significant, lower birthweight when compared with those born to women in the routine care group (four trials, 521 infants, mean difference (MD) -117.33 gram, 95% CI -198.72 to -35.94) (Analysis 1.6). Results from one trial also suggested that babies in the intervention group had slightly lower Ponderal Index when compared with babies in the routine care group (one trial, 300 infants, MD -0.09; 95% CI -0.16 to -0.02) (Bonomo 2005) (Analysis 1.7). No significant differences were seen in preterm birth (two trials, 138 infants, RR 1.00; 95% CI 0.26 to 3.82) (Analysis 1.8) or gestational age at birth (four trials, 521 infants, MD -0.18; 95% CI -0.43 to 0.07) (Analysis 1.9). There was no significant difference between the two groups in terms of admission to neonatal intensive care unit (two trials, 426 infants; RR 0.64; 95% CI 0.29 to 1.45) (Analysis 1.10), small for gestational age (three trials, 509 infants, RR 1.53; 95% CI 0.81 to 2.88) (Analysis 1.11) and shoulder dystocia (one trial, 83 infants, RR 0.69; 95% CI 0.06 to 7.27) (Analysis 1.12).

Two studies reported data on neonatal hypoglycaemia and hyperbilirubinaemia (Bonomo 2005; Langer 1989). Bonomo 2005 defined neonatal hypoglycaemia as BGL below 1.7 mmol/L in any two consecutive measurements and defined hyperbilirubinaemia as plasma bilirubin at least 205 μmol/l; while Langer 1989 defined neonatal hypoglycaemia as BGL below 1.94 mmol/L and defined hyperbilirubinaemia as plasma bilirubin at least 670 μmol/l. Substantial heterogeneity was detected for neonatal hypoglycaemia (I^2 = 62%, T^2 = 1.19) and hyperbilirubinaemia (I^2 = 50%, T^2 = 0.37), hence a random-effects meta-analysis was used for each outcome. There was no significant difference seen in the incidences of hypoglycaemia (two trials, 426 infants, RR 0.39; 95% CI 0.06 to 2.54) (Analysis 1.13) and hyperbilirubinaemia (two trials, 426 infants, RR 0.79; 95% CI 0.24 to 2.60) (Analysis 1.14).

There were no data reported on other fetal or neonatal secondary outcomes, and no data reported on childhood or adulthood outcomes.

For maternal secondary outcomes, women receiving interventions were more likely to have their labour induced when compared with women receiving routine care (one trial, 83 women, RR 17.69; 95% CI 1.03 to 304.09) (Analysis 1.15). Two studies reported data on maternal weight gain; however, there was no definition on maternal weight gain given (Bonomo 2005; Langer 1989). No significant difference was seen in weight gain during pregnancy (two trials, 426 women, MD -0.63 kg; 95% CI -3.07 to 1.81, I^2= 83%, T^2 = 2.60) (Analysis 1.16). Insulin or oral hypoglycaemic agent required for hyperglycaemia was reported in Grant 2011 with data available from 12 women, and there was no statistically significant difference between two groups (RR 1.00; 95% CI 0.30 to 3.32) (Analysis 1.17). Pre-eclampsia was only reported in Bevier 1999, and no significant difference was seen between two groups (83 women, RR 2.74; 95% CI 0.26 to 29.07) (Analysis 1.18). There were no data available on other maternal perinatal secondary outcomes and women's longer term health outcomes.

No trials reported data on health service cost.

Subgroup analyses and sensitivity analyses

Due to the small number of studies included and limited data available, no subgroup analyses and sensitivity analyses were conducted.

DISCUSSION

Summary of main results

In this review, we found that interventions including diet counselling, blood glucose monitoring and insulin therapy for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria significantly reduced the numbers of macrosomic and LGA babies. However, these benefits may be associated with an increased use of induction of labour for the mother, possibly due to awareness of the diagnosis of pregnancy hyperglycaemia by the attending health professionals.

Overall completeness and applicability of evidence

The evidence for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria is very incomplete.

The primary outcome of fetal/neonatal mortality was reported in only one pilot study (Grant 2011). There were no data available for maternal and child longer term outcomes and health service cost. With some reported secondary outcomes, including pre-eclampsia, insulin or oral hypoglycaemic agent required for hyperglycaemia, operative vaginal birth, induction of labour, shoulder dystocia, and ponderal index, evidence was based on data from a single trial.

Due to the small number of studies, moderate to high risk of bias of the included studies and small numbers of participants, the applicability of the current available evidence was limited. We have included only four small trials, with a total of 521 women and their babies in this review. All the four included trials were conducted in Western countries - Canada, Italy, and the United States.

Quality of the evidence

Three of the four included studies had moderate to high risk of bias (Bevier 1999; Bonomo 2005; Langer 1989). One study was with low risk of bias, but it accounted for limited weight in data analysis due to the small sample size of 12 women and babies.

Potential biases in the review process

The definition of the eligible population for this review may be a potential source of bias. We defined the review population as women with pregnancy hyperglycaemia not meeting gestational diabetes mellitus (GDM) and T2DM diagnostic criteria, and diagnostic criteria were defined by each individual trial. Due to the inconsistencies existing in GDM diagnosis around the world, we have included women with various degrees of pregnancy hyperglycaemia and may have included some women who could be diagnosed with GDM when using a different set of criteria.

Two of the four included trials had high risk of bias in incomplete outcome data (Bevier 1999; Bonomo 2005), which may have introduced attrition bias.

Agreements and disagreements with other studies or reviews

This review found that managing women with pregnancy hyperglycaemia not meeting GDM and T2DM diagnotic criteria was effective in reducing fetal overgrowth, without increasing the risks of instrumental birth, preterm birth, small-for-gestational age or admission to neonatal intensive care unit. These findings were inconsistent with results from large, well-designed randomised controlled trials (Crowther 2005; Landon 2009) and another Cochrane review on treatment for women with GDM (Alwan 2009).

The difference in caesarean section rate was not statistically different between the two groups in this review. Similar findings were reported in the Cochrane review (Alwan 2009) and in Crowther 2005. However, a significantly decreased caesarean section rate was found in women treated for GDM in Landon 2009.

In this review, data from a single trial suggested no statistically significant difference in the rate of pre-eclampsia between women in the two groups (Bevier 1999). Different findings were reported form the previous Cochrane review (Alwan 2009) and the large randomised controlled trials on treatment for women with GDM (Crowther 2005; Landon 2009), where a reduction in the risk of pre-eclampsia was found by managing women with GDM. The disagreement may result from the limited data included in this review for this outcome measure.

AUTHORS' CONCLUSIONS

Implications for practice

This review found interventions for women with pregnancy hyperglycaemia not meeting GDM and T2DM diagnostic criteria helped reduce the number of macrosomic and LGA babies. It is important to note that the results of this review were based on four small randomised trials with moderate to high risk of bias without follow-up outcomes for women or their babies. Until additional evidence from large well designed randomised trials becomes available, current evidence is insufficient to make conclusive suggestions on management for women with pregnancy hyperglycaemia not meeting GDM and T2DM diagnostic criteria.

Implications for research

Further larger trials with sufficient power to assess the effects of lifestyle intervention and metabolic monitoring on maternal and infant health outcomes are needed. Outcomes such as longer term

health outcomes for women and their babies after being managed for pregnancy hyperglycaemia during pregnancy and health service cost should be included.

ACKNOWLEDGEMENTS

Thanks to Professor Thomas Wolever for providing additional information and subgroup data.

As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team) and the Group's Statistical Adviser.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Bevier 1999

Methods	Randomised controlled trial.
Participants	103 women with a positive 50 g 1-hour GCT (> 140 mg/dl) but a negative 100 g 3-hour OGTT according to the National Diabetes Data Group (NDDG) criteria (see notes) Exclusion criteria: women with evidence of hypertension, collagen disease, chronic renal disease, cardiac or pulmonary disease, Rh sensitisation, or a history of preterm labor or SGA infants Setting: Santa Barbara, California, USA.
Interventions	• Women in the intervention group (n = 35) 1. Dietary counselling: 30 kcal/kg/day if woman was 80-120% of ideal body weight; or 24 kcal/kg/day if woman was greater than 120% of ideal body weight; diet consisted of 40% carbohydrate, 20% protein, and 40% fat, broken into 3 meals and 3 snacks. 2. Home blood glucose monitoring (HBGM) instruction: checking the fasting and the 1-hr postprandial BGL, using visual reagent strips. Weekly HBGM diary to clinic. 3. Weekly random BGL at clinic. 4. Weekly reinforcement of prescribed diet. 5. Insulin therapy when fasting BGL > 90 mg/dl or the 1-hr BGL > 120 mg/dl on 3 or more occasions. • Women in the control group (n = 48) 1. Random BGL during regular clinic visits. 2. Insulin therapy when the random result > 120 mg/dl. • All women had haemoglobin A_{1c} (HbA_{1c}) measurement at 28 and 32 weeks.
Outcomes	Maternal HbA1c level, pre-eclampsia, mode of birth, delivery complications (shoulder dystocia, tight nuchal cord, meconium, prolonged labor phase, abnormal fetal heart rate), gestational age at birth, Apgar score at 1 min and 5 min, birthweight, infant haemoglobin, glucose, haematocrit, morbidities, and congenital anomalies
Notes	• The NDDG criteria (adopted by ADA and ACOG at the time of study) 1. Fasting: > 105 mg/dl (5.8 mmol/l). 2. 1-h: > 190 mg/dl (10.6 mmol/l). 3. 2-h: > 165 mg/dl (9.2 mmol/l). 4. 3-h: > 145 mg/dl (8.1 mmol/l). 5. 2 or more of the values must be met or exceeded for GDM diagnosis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as women were randomly assigned to either experimental or control groups
Allocation concealment (selection bias)	Unclear risk	No information was given on allocation concealment.

Bevier 1999 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Prenatal care and deliveries were performed by six obstetricians who were not blinded to the mothers treatment group Participants were unlikely to be blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on whether outcome assessors were blinded or not
Incomplete outcome data (attrition bias) All outcomes	High risk	• A total of 20 women (19.4%) were excluded post randomisation 1. 5 women (4 in control group, 1 in experimental group) required insulin. 2. 1 women had a therapeutic abortion. 3. 14 women were noncompliant to allocated treatment (i.e. women in the intervention group did not adhere to intervention or women in the control group received diet counselling and/or home blood glucose monitoring instructions). • 83 women (45 in the control group and 35 in the intervention group) were included in analysis.
Selective reporting (reporting bias)	High risk	There was no clear definition on macrosomia. Published data on macrosomia was unclear, and cannot be included in the meta-analysis of macrosomia
Other bias	Low risk	No obvious risk of other bias.

Bonomo 2005

Methods	Randomised controlled trial.
Participants	300 Caucasian women with singleton pregnancies, with a positive 50 gram 1-hour GCT test (≥ 7.8 mmol/l) followed by a normal 100-gram OGTT according to Carpenter and Coustan's criteria (see notes) Women with one abnormal value at the 100-gram OGTT or fulfilling Carpenter and Coustan's diagnostic criteria for GDM were excluded Setting: The Diabetic and Pregnancy Centre of Niguarda Ca'Granda' Hospital in Milan, Italy
Interventions	• Women in the intervention group (n = 150) 1. Dietary advice providing 24-30 kcal /kg per day, based on prepregnancy body weight; caloric intake was divided into three meals and 2 or 3 snacks, and distributed as 50-55% carbohydrate, 25-30% protein, 20-25% fat. 2. Out-patient management protocol: visits every 2 weeks, when the main clinical parameters (weight, blood pressure) were recorded, discussion of dietary habits with evaluation of therapeutic compliance, and measurement of fasting and 2-h postprandial blood glucose, of HbA1c and fructosamine.

	3. Urine test every morning at home for ketone bodies. • Women in the control group (n = 150) 1. Women were reassured after testing. 2. No special care, diet, or pharmacological treatment.
Outcomes	Maternal: caesarean section; infant: gestational age at delivery, birthweight, macrosomia (birthweight ≥ 4000 g), LGA (birthweight ≥ 90th centile), SGA (birthweight ≤ 10th centile), ponderal index, hypoglycaemia (any of 2 consecutive blood glucose values < 1. 7 mmol/l), hyperbilirubinaemia (plasma values ≥ 205 µmol/l), polycythaemia (haematocrit > 60%), 5-min Apgar score < 7, admission to neonatal intensive care unit
Notes	• Carpenter and Coustan's diagnostic criteria 1. Fasting: 5.3 mmol/L. 2. 1-hour: 10.0 mmol/l. 3. 2-hour: 8.6 mmol/l. 4. 3-hour: 7.8 mmol/l. 5. 2 or more results equal to or greater than the cut-off values is required for a diagnosis of GDM. • Blood glucose targets were < 5 mmol/l fasting, and < 6.7 mmol/l 2-h postprandial for women in the intervention group.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Described as randomly assigned to 1 of the 2 study groups, no other information available
Allocation concealment (selection bias)	Unclear risk	No information was given on allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	All women, and the attending physicians were informed of the results of the GCT and OGTT. It is unclear whether research personnel are blinded from knowledge of group allocation; participants were unlikely to be blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on whether the outcome assessors were blinded or not
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses to follow-up (2%): 6 women in the intervention group loss to follow-up Post-randomisation exclusion (5%): 9 women in intervention group and 6 in the control group were excluded due to the diagnosis of GDM at 30-34 weeks' gestation All those women were described as "replaced".
Selective reporting (reporting bias)	Low risk	No obvious risk of selective reporting.

Other bias	Low risk	No obvious risk of other bias.

Grant 2011

Methods	Randomised controlled pilot study.
Participants	12 pregnant women 18-45 years of age, diagnosed with impaired glucose tolerance of pregnancy (IGTP) according to Canadian Diabetes Association (CDA) criteria, and who had been referred to the Diabetes in Pregnancy Clinic (DIP), St. Michael's Hospital, Canada Exclusion criteria: presence of a multiple pregnancy or an acute or chronic illness affecting carbohydrate metabolism; presence of type 1 or type 2 diabetes prior to the current pregnancy; use of insulin treatment prior to providing consent; greater than 34 weeks' gestation; and unable to communicate in English with no translator available
Interventions	• Women in the intervention group (n = 8): to select their starch choices from an exchange list of low glycaemic index (GI) foods. • Women in the control group (n = 4): to select starch choices from an exchange list of intermediate- and high-GI foods, reflecting the usual intake of typical Diabetes in Pregnancy Clinic (DIP) patients. • All women: standard medical nutrition therapy for patients with gestational diabetes followed within the DIP clinic (patients were introduced to the Diabetes Food Guide and Canadian dietary recommendations to support a healthy pregnancy. Clinic dietician recommended how many starch choices/servings each participant should consume at each mean based upon their own individual gestational energy requirements and Acceptable Macronutrient Distribution Ranges. Free-of-charge, with approximately $20/week worth of non-perishable study foods and all blood testing strips. Self-monitored blood glucose (SMBG) from baseline to week 8; 4 times/day (fasting, 2-h after breakfast, lunch and dinner); Insulin therapy if SMBG were not met with lifestyle modification within 2-3 weeks.
Outcomes	Primary: fasting serum glucose and HbA1c levels at baseline and 4 weeks; self-monitored blood glucose level (SMBG) from baseline to week 8 Secondary: serum glucose level, insulin, lipids and C-reactive protein at baseline and 4 weeks after intervention, maternal dietary intake, physical activity (time, type and duration), birthweight, use of insulin, macrosomia (birthweight $\geq$ 4000 g), LGA (> 90 th percentile population specific), SGA (< 10th percentile population specific).
Notes	• CDA GDM diagnostic criteria 1. Fasting: 5.3 mmol/L. 2. 1-h 75-g OGTT: 10.6mmol/L. 3. 2-h 75-g OGTT: 8.9mmol/L. 4. IGTP: 1 of the values is met or exceeded. 5. GDM: 2 of the values are met or exceeded.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Grant 2011 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Randomisation order was created by 1 of the investigators who was not involved in recruitment. It is unclear how the sequence was generated, but it is likely to be computer-generated sequence
Allocation concealment (selection bias)	Low risk	Sealed, numbered, opaque envelopes were used, and various block sizes in randomisation were used
Blinding of participants and personnel (performance bias) All outcomes	High risk	Described as an "open-label" pilot study.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women in the control group withdrew after randomisation, reasons given
Selective reporting (reporting bias)	Low risk	No obvious risk of selective reporting.
Other bias	Low risk	There is no obvious risk of other bias.

Langer 1989

Methods	Randomised controlled trial.
Participants	126 women with a positive 50 g 1-hour GCT (≥130 mg/dl) and with one abnormal value in 100 g 3-hour OGTT according to NDDG criteria Setting: Bronx, New York, USA.
Interventions	• Women (n = 63) in the intervention group 1. Capillary blood glucose monitoring: 7 times a day. 2. Diabetic management protocol: 25 kcal/kg/day for women pre-pregnancy BMI ≥ 27 kg/m^2 and 30 kcal/kg/day for women pre-pregnancy BMI < 27 kg/m^2. 3. Insulin therapy when diet alone is not able to achieve the tight glycaemic control of 95 mg/dl. The insulin dose was calculated based on 0.7 U of insulin per kg of body weight measured in pregnancy. Human insulin was administered by multiple insulin injection regimen. The standard formula for the amount of insulin prescribed was two thirds of all insulin in the morning (2:1, intermediate-acting/ regular insulin) and one third in the evening (1:1. regular/intermediate-acting). • Women (n = 63) in the control group 1. Habitual routine diet. 2. Capillary BGL monitoring for a baseline period of 4 weeks.

Langer 1989 (*Continued*)

Outcomes	Maternal: gestational age at delivery, weight gain, caesarean section; hypertensive disorders Infant: birthweight, LGA (birthweight $\geq 90^{th}$ Centile); SGA (birthweight $\leq 10^{th}$ centile); preterm birth (< 37 weeks' gestation); hypoglycaemia (BGL < 35 mg/dl or 1.94 mmol/l); hyperbilirubinaemia (bilirubin > 12 mg/dl); hypocalcaemia (calcium < 7.5 mg/dl); polycythemia (central venous hematocrit > 62%); admission to neonatal intensive care unit; respiratory distress syndrome
Notes	• The NDDG criteria (adopted by ADA and ACOG at the time of study) 1. Fasting: > 105 mg/dl (5.8 mmol/l). 2. 1-h: > 190 mg/dl (10.6 mmol/l). 3. 2-h: > 165 mg/dl (9.2 mmol/l). 4. 3-h: > 145 mg/dl (8.1 mmol/l). 5. 2 or more of the values must be met or exceeded for GDM diagnosis. • All women were instructed to add 150 g of carbohydrate to their usual meals for each of 3 days before their 100-g OGTT.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Described as "randomised into treated and untreated groups."
Allocation concealment (selection bias)	Unclear risk	No information was given on allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	It is unlikely to blind study participants. No information on whether research personnel was blinded or not
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information about whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up or post randomisation exclusion.
Selective reporting (reporting bias)	Low risk	No obvious risk of selective reporting.
Other bias	Low risk	No obvious risk of other bias.

ACOG: American Congress of Obstetricians and Gynecologists (formerly the American College of Obstetricians and Gynecologists)
ADA: American Diabetes Association
BGL: blood glucose level
GCT: glucose challenge test
GDM: gestational diabetes mellitus
GI: glycaemic index

IGTP: impaired glucose tolerance of pregnancy
LGA: large for gestational age
NDDG: National Diabetes Data Group
OGTT: oral glucose tolerance test

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bung 1993	Diagnosis of "disturbed carbohydrate metabolism during pregnancy" was based on fasting plasma glucose values but not on OGTT results
Dunne 2001	No published or unpublished data available.
Ford 1997	Participants were women with GDM as defined by WHO 1980 criteria (2-hour BGL between 8 mmol/L and 11 mmol/L in 75-gram OGTT)
Li 1987	Participants were women with GDM according to NDDG criteria and group allocation is based on alternation
Li 1999	Not a randomised trial, group allocation is based on alternation
Maresh 1983	Not a randomised trial, group allocation by alternation.
Yang 2003	Participants were women with GDM according to WHO criteria (2-hour BGL between 7.8 and 11.1 mmol/L in 75-gram OGTT)

BGL: blood glucose level
GDM: gestational diabetes mellitus
NDDG: National Diabetes Data Group
OGTT: oral glucose tolerance test

Characteristics of ongoing studies *[ordered by study ID]*

Crowther 2007

Trial name or title	Investigation of dietary and lifestyle advice for women with borderline gestational glucose intolerance (IDEAL study)
Methods	Randomised clinical trial.
Participants	Pregnant women with a singleton pregnancy, with a positive 50 g OGCT (1-h BGL $\geq$ 7.8 mmol/L) and a normal 2-h 75 g OGTT (fasting BGL < 5.5 mmol/L and 2-h BGL < 7.8 mmol/L)
Interventions	Lifestyle counselling (individualised diet and exercise advice from a registered dietitian based on published recommendations of the Dietitians Association of Australia), BGL monitoring and insulin therapy if necessary

Crowther 2007 (*Continued*)

Outcomes	LGA, death or serious health outcome for the infant, other causes of infant morbidity (e.g. macrosomia, SGA, neonatal hypoglycaemia requiring treatment, shoulder dystocia, nerve palsy, bone fracture, preterm birth, Apgar score < 7 at 5 minutes), serious or adverse health outcomes for the women (e.g. maternal death, pre-eclampsia, caesarean birth, induction of labour, antepartum/ postpartum haemorrhage, weight gain ≥10 kg in pregnancy, need for antenatal hospitalisation), maternal psychological outcomes and health status, use of hospital services and health costs
Starting date	2008.
Contact information	Caroline.crowther@adelaide.edu.au
Notes	

Wolever 2011 [pers comm]

Trial name or title	
Methods	Randomised clinical trial.
Participants	Women with GDM and IGTP.
Interventions	Low-glycaemic index diet will be compared with control diet (intermediate- and high-glycaemic index diet)
Outcomes	Primary: fasting serum glucose and HbA1c levels at baseline and 4 weeks; self-monitored blood glucose level from baseline to week 8
Starting date	Not yet recruiting.
Contact information	Thomas.wolever@utoronto.ca
Notes	

BGL: blood glucose level
GDM: gestational diabetes mellitus
IGTP: impaired glucose tolerance of pregnancy
LGA: large for gestational age
OGTT: oral glucose tolerance test
SGA: small for gestational age

DATA AND ANALYSES

Comparison 1. Intensive management versus routine care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Large-for-gestational age	3	438	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.20, 0.66]
2 Macrosomia	3	438	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.19, 0.74]
3 Large-for-gestational age or macrosomia	1	83	Risk Ratio (M-H, Fixed, 95% CI)	0.11 [0.02, 0.84]
4 Caesarean section	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Any caesarean section	3	509	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.68, 1.27]
4.2 Primary caesarean section	2	209	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.42, 2.33]
4.3 Repeat caesarean section	2	209	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.17, 1.26]
5 Operative vaginal delivery	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Unspecified	1	83	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [0.20, 9.27]
5.2 Vacuum	1	83	Risk Ratio (M-H, Fixed, 95% CI)	2.74 [0.26, 29.07]
5.3 Forceps	1	83	Risk Ratio (M-H, Fixed, 95% CI)	0.45 [0.02, 10.82]
6 Birthweight (gram)	4	521	Mean Difference (IV, Fixed, 95% CI)	-117.33 [-198.72, -35.94]
7 Ponderal index (gram x 100/m^3)	1	300	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.16, -0.02]
8 Preterm birth	2	138	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.26, 3.82]
9 Gestational age at birth (week)	4	521	Mean Difference (IV, Fixed, 95% CI)	-0.18 [-0.43, 0.07]
10 Admission to neonatal intensive care unit	2	426	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.29, 1.45]
11 Small-for-gestational age	3	509	Risk Ratio (M-H, Fixed, 95% CI)	1.53 [0.81, 2.88]
12 Shoulder dystocia	1	83	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.06, 7.27]
13 Neonatal hypoglycaemia	2	426	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.06, 2.54]
14 Hyperbilirubinaemia	2	426	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.24, 2.60]
15 Induction of labour	1	83	Risk Ratio (M-H, Fixed, 95% CI)	17.69 [1.03, 304.09]
16 Weight gain during pregnancy (kg)	2	426	Mean Difference (IV, Random, 95% CI)	-0.63 [-3.07, 1.81]
17 insulin or oral hypoglycaemic agent required for hyperglycaemia	1	12	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.30, 3.32]
18 Pre-eclampsia	1	83	Risk Ratio (M-H, Fixed, 95% CI)	2.74 [0.26, 29.07]

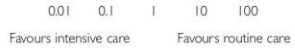
Analysis 1.1. Comparison 1 Intensive management versus routine care, Outcome 1 Large-for-gestational age.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 1 Large-for-gestational age

Study or subgroup	Intensive care n/N	Routine care n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Grant 2011	1/8	1/4		3.6 %	0.50 [0.04, 6.08]
Langer 1989	4/63	15/63		40.2 %	0.27 [0.09, 0.76]
Bonomo 2005	9/150	21/150		56.2 %	0.43 [0.20, 0.90]
Total (95% CI)	**221**	**217**		**100.0 %**	**0.37 [0.20, 0.66]**
Total events: 14 (Intensive care), 37 (Routine care)					
Heterogeneity: Chi^2 = 0.58, df = 2 (P = 0.75); I^2 =0.0%					
Test for overall effect: Z = 3.35 (P = 0.00082)					
Test for subgroup differences: Not applicable					

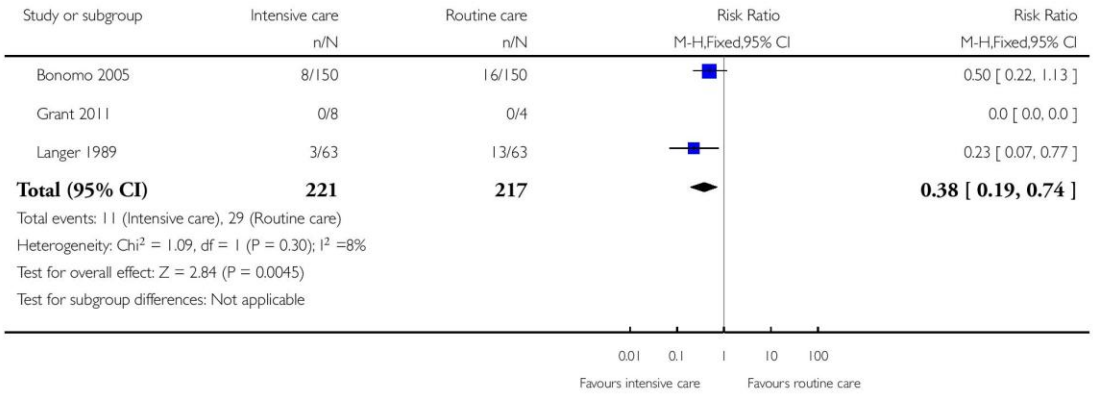


Analysis 1.2. Comparison 1 Intensive management versus routine care, Outcome 2 Macrosomia.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 2 Macrosomia

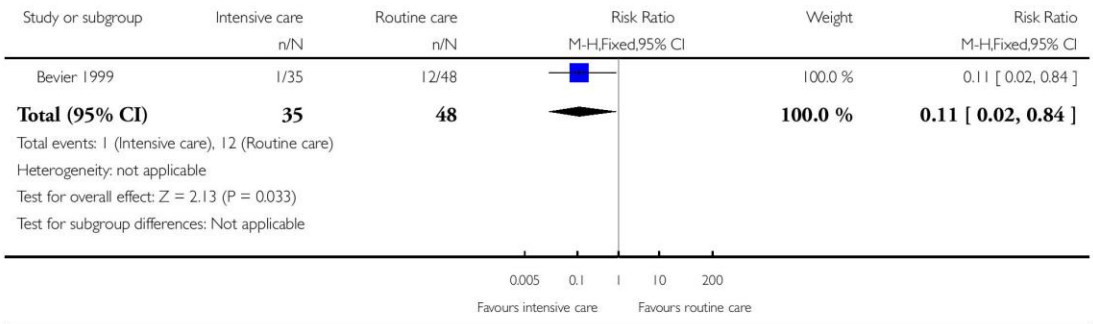


Analysis 1.3. Comparison 1 Intensive management versus routine care, Outcome 3 Large-for-gestational age or macrosomia.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 3 Large-for-gestational age or macrosomia

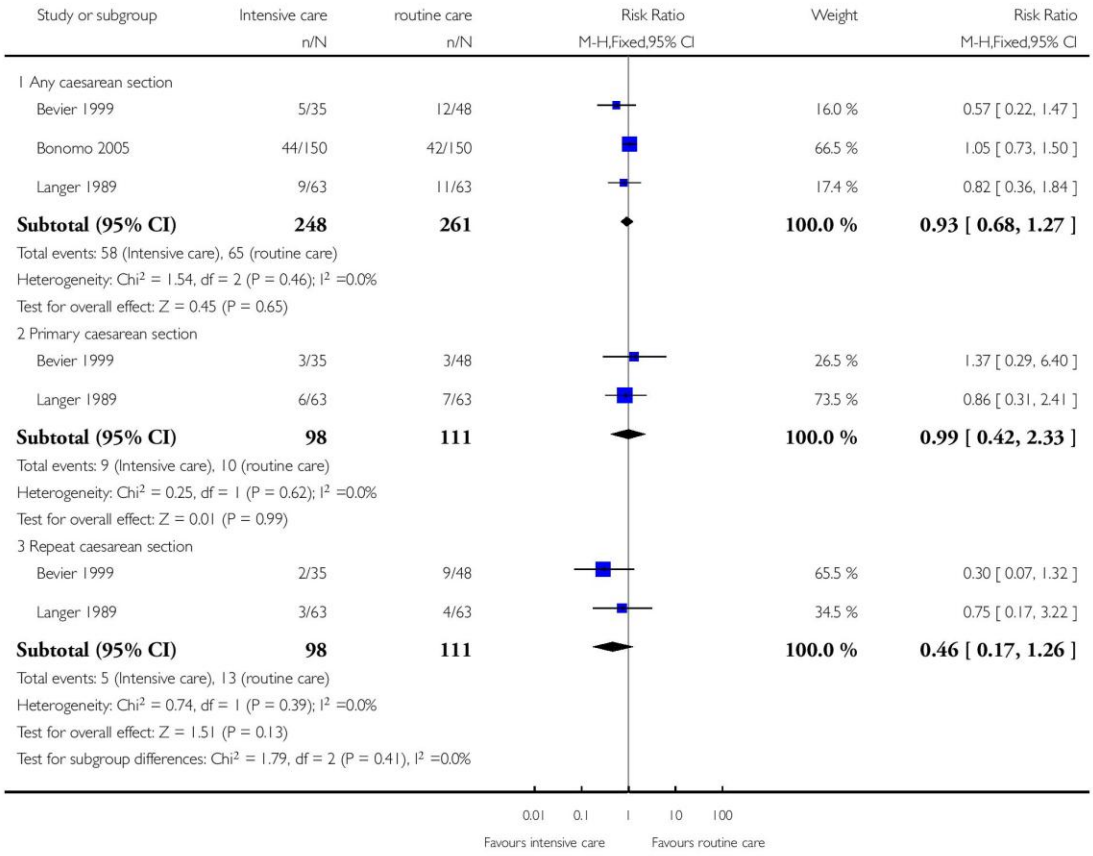


Analysis 1.4. Comparison 1 Intensive management versus routine care, Outcome 4 Caesarean section.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 4 Caesarean section

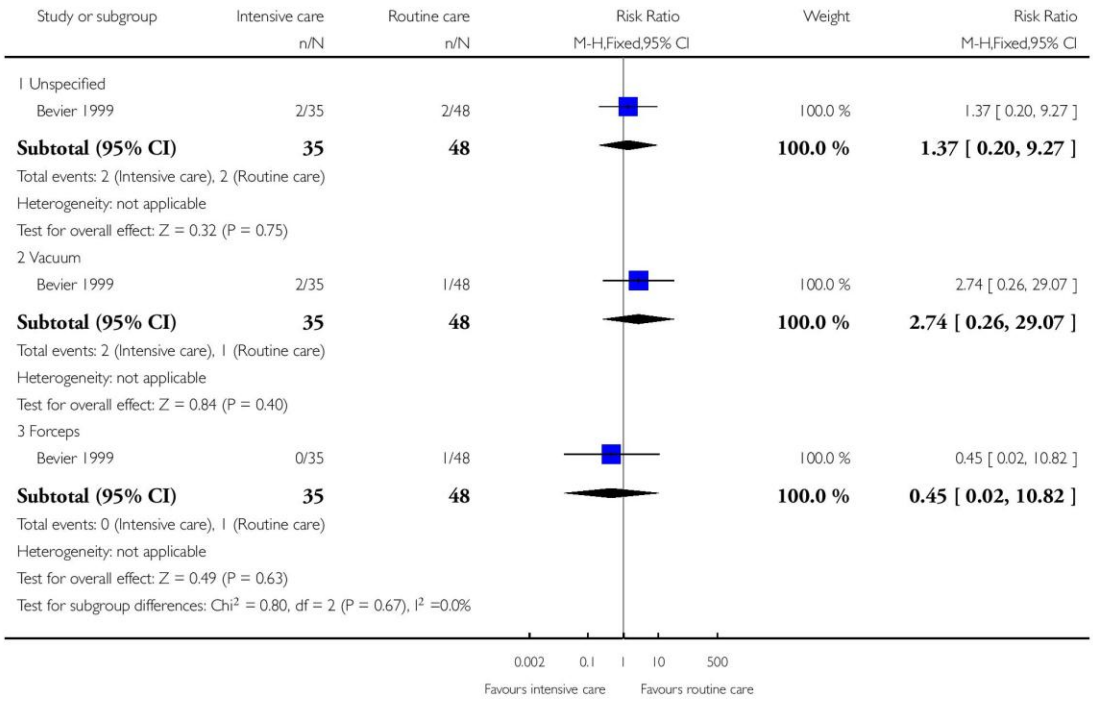


Analysis 1.5. Comparison 1 Intensive management versus routine care, Outcome 5 Operative vaginal delivery.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 5 Operative vaginal delivery

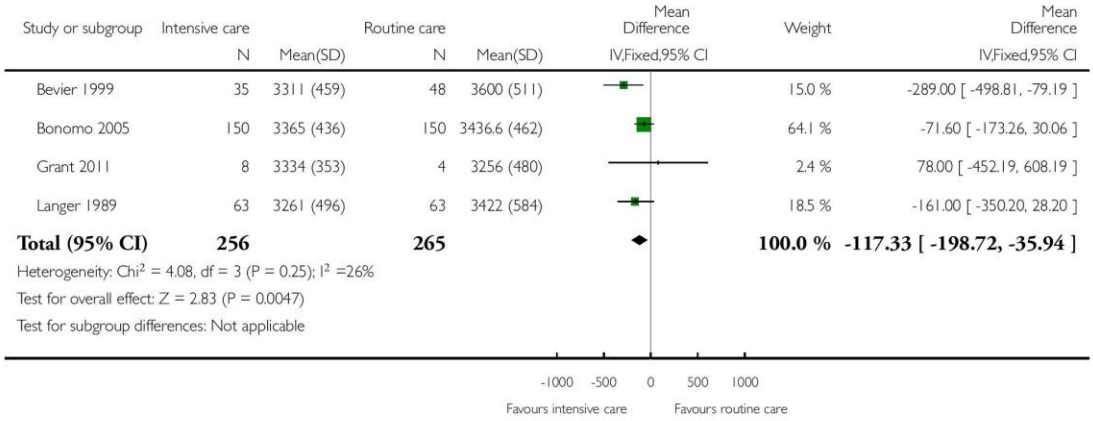


Analysis 1.6. Comparison 1 Intensive management versus routine care, Outcome 6 Birthweight (gram).

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 6 Birthweight (gram)

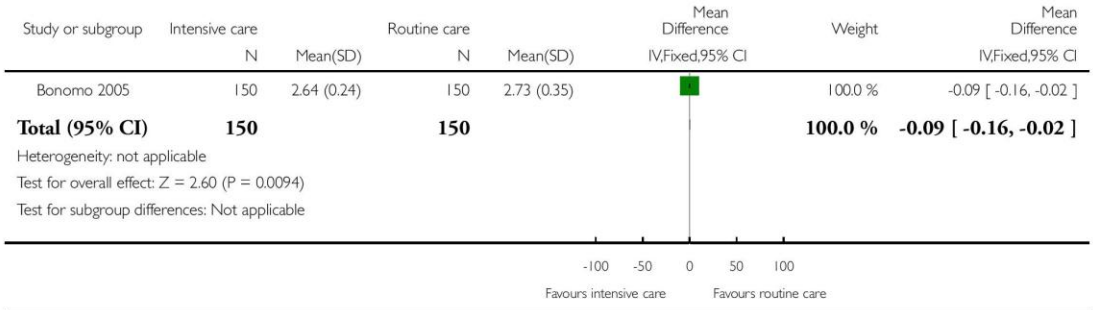


Analysis 1.7. Comparison 1 Intensive management versus routine care, Outcome 7 Ponderal index (gram x 100/m3).

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 7 Ponderal index (gram x 100/m^3)

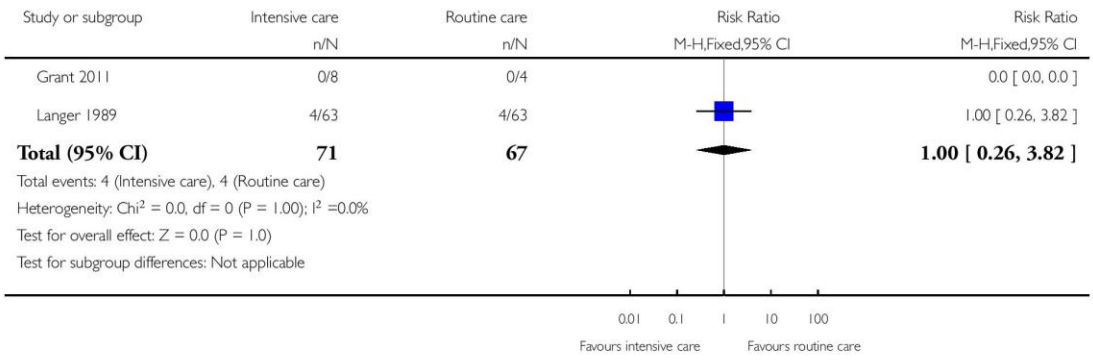


Analysis 1.8. Comparison 1 Intensive management versus routine care, Outcome 8 Preterm birth.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 8 Preterm birth

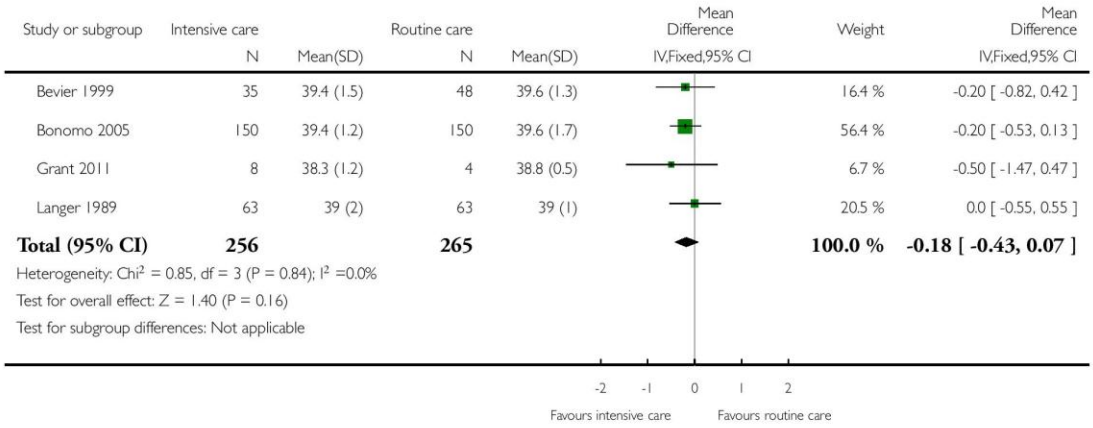


Analysis 1.9. Comparison 1 Intensive management versus routine care, Outcome 9 Gestational age at birth (week).

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 9 Gestational age at birth (week)



Analysis 1.10. Comparison 1 Intensive management versus routine care, Outcome 10 Admission to neonatal intensive care unit.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 10 Admission to neonatal intensive care unit

Study or subgroup	Intensive care n/N	Routine care n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Bonomo 2005	5/150	7/150		50.0 %	0.71 [0.23, 2.20]
Langer 1989	4/63	7/63		50.0 %	0.57 [0.18, 1.86]
Total (95% CI)	**213**	**213**		**100.0 %**	**0.64 [0.29, 1.45]**

Total events: 9 (Intensive care), 14 (Routine care)
Heterogeneity: $Chi^2 = 0.07$, df = 1 (P = 0.79); $I^2 = 0.0\%$
Test for overall effect: Z = 1.07 (P = 0.29)
Test for subgroup differences: Not applicable

Analysis 1.11. Comparison 1 Intensive management versus routine care, Outcome 11 Small-for-gestational age.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 11 Small-for-gestational age

Study or subgroup	Intensive care n/N	Routine care n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Bevier 1999	3/35	2/48		11.5 %	2.06 [0.36, 11.67]
Bonomo 2005	13/150	9/150		61.3 %	1.44 [0.64, 3.28]
Langer 1989	6/63	4/63		27.2 %	1.50 [0.44, 5.06]
Total (95% CI)	**248**	**261**		**100.0 %**	**1.53 [0.81, 2.88]**

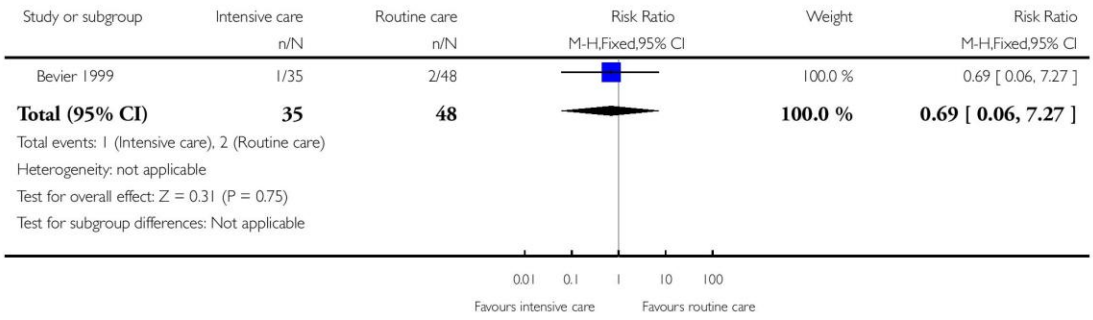
Total events: 22 (Intensive care), 15 (Routine care)
Heterogeneity: $Chi^2 = 0.13$, df = 2 (P = 0.94); $I^2 = 0.0\%$
Test for overall effect: Z = 1.32 (P = 0.19)
Test for subgroup differences: Not applicable

Analysis 1.12. Comparison 1 Intensive management versus routine care, Outcome 12 Shoulder dystocia.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 12 Shoulder dystocia

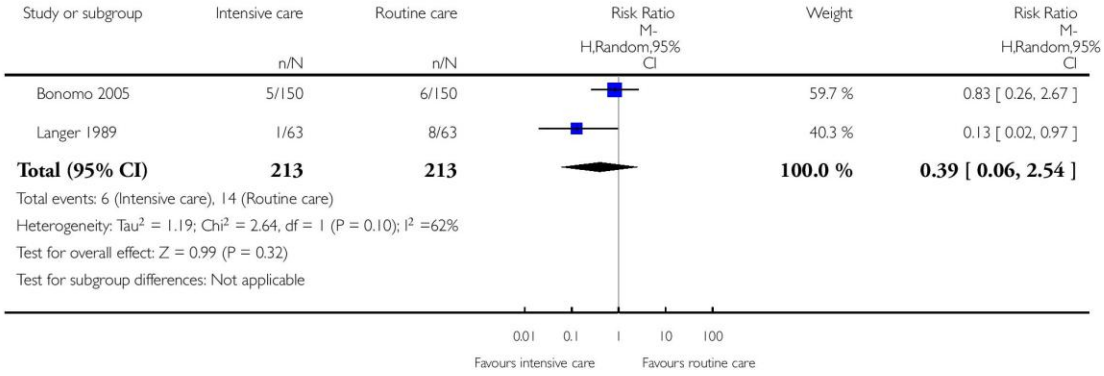


Analysis 1.13. Comparison 1 Intensive management versus routine care, Outcome 13 Neonatal hypoglycaemia.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 13 Neonatal hypoglycaemia

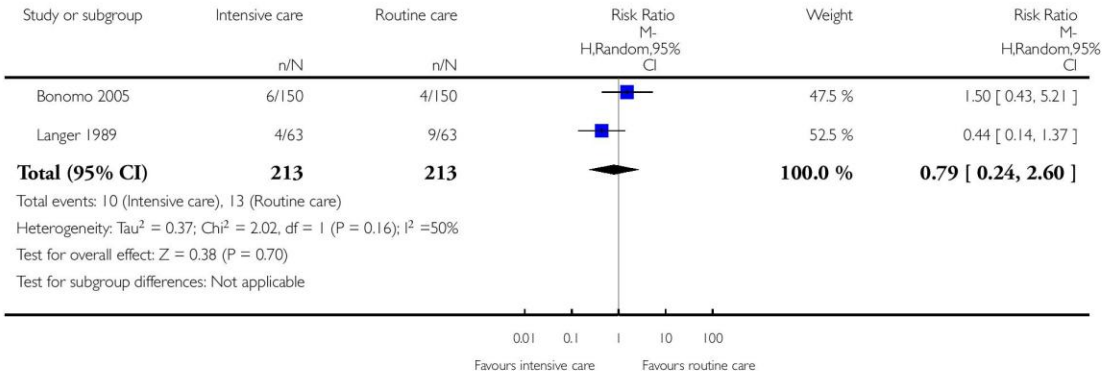


Analysis 1.14. Comparison 1 Intensive management versus routine care, Outcome 14 Hyperbilirubinaemia.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 14 Hyperbilirubinaemia

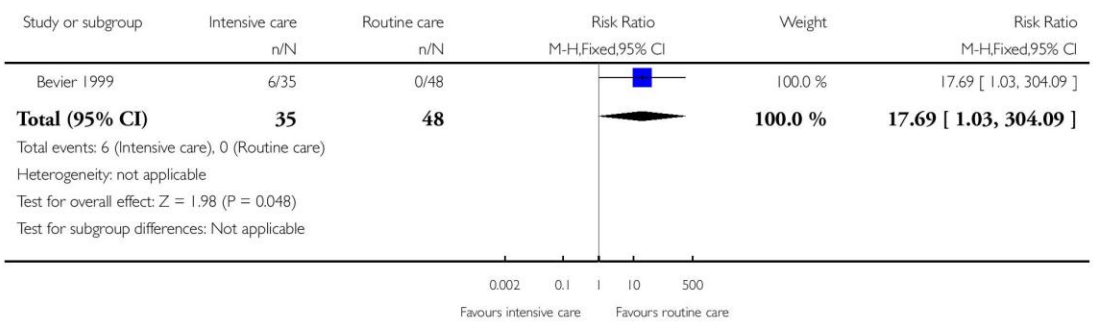


Analysis 1.15. Comparison 1 Intensive management versus routine care, Outcome 15 Induction of labour.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 15 Induction of labour

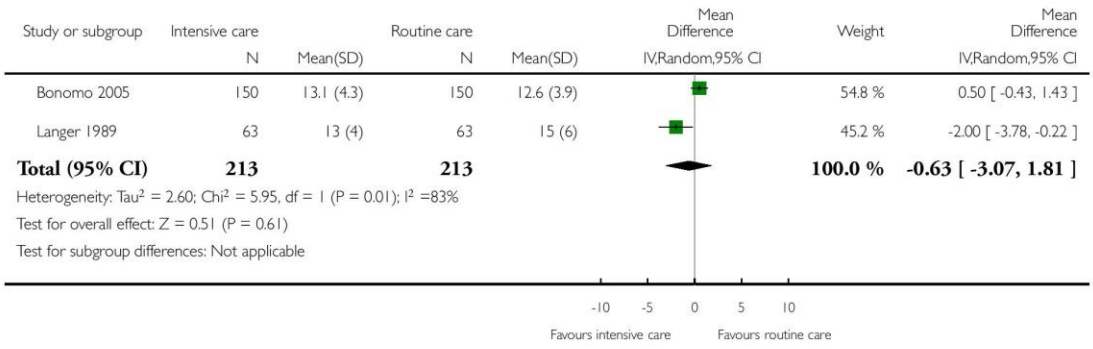


Analysis 1.16. Comparison 1 Intensive management versus routine care, Outcome 16 Weight gain during pregnancy (kg).

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 16 Weight gain during pregnancy (kg)

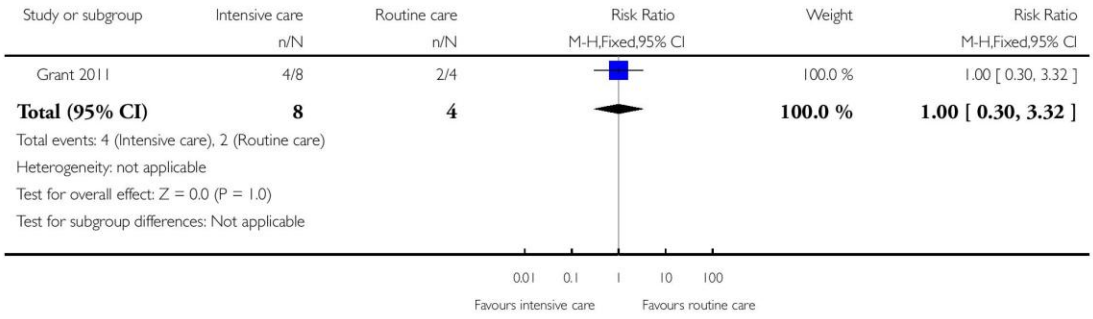


Analysis 1.17. Comparison 1 Intensive management versus routine care, Outcome 17 insulin or oral hypoglycaemic agent required for hyperglycaemia.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 17 insulin or oral hypoglycaemic agent required for hyperglycaemia

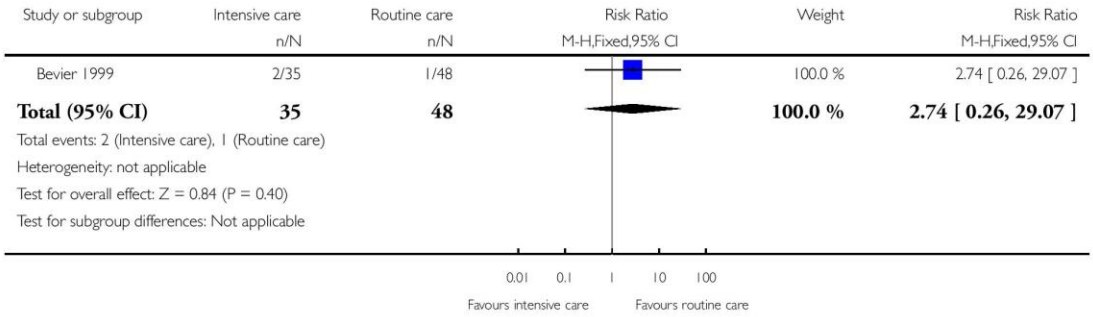


Analysis 1.18. Comparison 1 Intensive management versus routine care, Outcome 18 Pre-eclampsia.

Review: Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Comparison: 1 Intensive management versus routine care

Outcome: 18 Pre-eclampsia



WHAT'S NEW

Last assessed as up-to-date: 21 November 2011.

Date	Event	Description
18 April 2012	Amended	Corrected typographical error in Agreements and disagreements with other studies or reviews.

HISTORY

Protocol first published: Issue 3, 2011

Review first published: Issue 1, 2012

CONTRIBUTIONS OF AUTHORS

Shanshan Han wrote drafts of the protocol and review, with Caroline Crowther and Philippa Middleton contributing to data extraction, and commenting on and editing to all drafts.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- ARCH, Robinson Institute, The University of Adelaide, Australia.

External sources

- Australian Department of Health and Ageing, Australia.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

A combined outcome of 'large-for-gestational age or macrosomia' was added in the review.

INDEX TERMS

Medical Subject Headings (MeSH)

Blood Glucose [analysis]; Cesarean Section [utilization]; Diabetes Mellitus, Type 2 [blood; *diagnosis]; Diabetes, Gestational [blood; *diagnosis]; Fetal Macrosomia [prevention & control]; Glucose Tolerance Test; Hyperglycemia [diet therapy; *therapy]; Hypoglycemic Agents [therapeutic use]; Infant, Newborn; Infant, Postmature; Insulin [therapeutic use]; Patient Education as Topic; Pregnancy Complications [blood; diet therapy; *therapy]; Pregnant Women; Publication Bias; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Pregnancy

5 A qualitative study of women's views on their diagnosis and management for borderline gestational diabetes mellitus

5.1 Background

Gestational diabetes mellitus (GDM) is defined as glucose intolerance or hyperglycaemia with onset or first recognition during pregnancy (Metzger and Coustan 1998). GDM is one of the most common complications of pregnancy, with prevalence varying between 1% and 14% around the world (Mulla et al 2010). The prevalence of GDM continues to increase in line with the increasing prevalence of maternal obesity and type 2 diabetes mellitus (T2DM) (Bottalico 2007; Debelea et al 2005; Ferrara 2007).

Maternal pregnancy hyperglycaemia has a continuous relationship with adverse pregnancy outcomes, including large for gestational age infant, neonatal hypoglycaemia, preterm birth, shoulder dystocia, caesarean section and preeclampsia (IADPSG 2010) (HAPO Study Cooperative Research Group 2009). Although GDM usually resolves after birth, up to 50% of women with a history of GDM will develop T2DM within 10 years of the index pregnancy (Kim et al 2002).

Behavioural management, involving dietary and lifestyle interventions, has been found beneficial and is usually recommended as the primary therapeutic strategy for managing pregnancy hyperglycaemia (Alwan et al 2009; Han et al 2012a). In-depth understanding of psychosocial factors that determine an individual's behaviour are therefore important in the development of tailored lifestyle interventions for women with pregnancy hyperglycaemia. This may greatly improve the effectiveness of the care provided (Bowling 2002; Nolan et al 2011).

Evidence from previous questionnaire based studies suggest women with a positive oral glucose challenge test (OGCT) but a normal oral glucose tolerance test (OGTT) were less likely to perceive their health as "excellent" when compared with women with normal glycaemia during pregnancy (Kerbel et al 1997; Rumbold and Crowther 2002). However, little is known about their views towards receiving lifestyle management advice or about factors that may influence their ability to make behavioural changes.

This qualitative study, nested within a study of "investigation of dietary and lifestyle advice for women with borderline gestational diabetes " (Crowther et al 2012), aimed to explore women's experiences after being diagnosed with borderline GDM, their attitudes towards management, and to identify factors important to them in achieving any intended lifestyle changes. Borderline GDM was defined as a positive 50g oral glucose challenge test (OGCT) (1 hour venous plasma glucose ≥7.8 mmol/L) followed by a normal oral 75 g glucose tolerance test (OGTT) (fasting venous plasma glucose <5.5 mmol/L and a 2 hour glucose <7.8 mmol/L) (Crowther et al 2012).

5.2 Methods

5.2.1 **Participants and procedure**

Women were eligible if they were participants in the IDEAL study (Crowther et al 2012), either from the intervention group who received diet and exercise advice for managing borderline GDM or the routine-care group, able to communicate in English and within two weeks after trial entry or less than 12 months postpartum. Women who developed GDM or were diagnosed with T2DM during the study period were not eligible for this qualitative study. Women were recruited at the Women's and Children's Hospital (WCH), Adelaide, a Level 3 teaching hospital, either face-to-face or via the telephone using a purposive sampling method. During the recruitment process, women

were made aware that the interview was not for assessment of their knowledge or skill and would not affect their care by their attending clinical team. They were advised that information collected during the interview would be kept confidential and anonymous. We aimed to recruit between 16 to 20 women for the qualitative interview, to reach data saturation in the thematic analysis when no further new themes or sub-themes would be revealed (Guest et al 2006).

5.2.2 **The interview**

Semi-structured, face-to-face interviews, to facilitate a deeper understanding (Flick 2009), were conducted by a single researcher (the candidate Shanshan Han) with training in interview skills. Interviews were conducted in a quiet office away from the busy hospital clinic area. No explicit time restraints were applied, with each interview typically taking about 25 minutes.

A semi-structured topic list was prepared and pilot tested before the interview (Appendix 9.1). The topics were designed to explore the woman's feelings and experiences about a diagnosis of borderline GDM and its subsequent management, as well as factors that might affect their ability to change behaviours. By the end of each interview, a brief summary of the interview was given to the women by the interviewer to check if anything significant had been missed or if there was any misinterpretation.

Analysis

Each interview was audio tape recorded and transcribed verbatim by two people not involved in the study (Elen Shute and Claire Binnion). Field notes and interview summaries were prepared immediately after each interview by the interviewer (Shanshan Han) to help later analysis.

The transcripts of the interviews were analysed using the content analysis methods based on Graneheim and Lundman (Graneheim and Lundman 2004). To satisfy reliability criteria, the interview transcripts were read and coded by two investigators (Tanya Bubner and Shanshan Han) independently. Any discrepancies on categorisation were solved by discussion and/or consultation with third independent investigator (Philippa Middleton).

Transcribed data for the different interviews were analysed thematically by systematic comparisons, derived from grounded theory method (Glaser and Strauss 1967) and were organised by themes. Themes were then coded into categories. Data about enablers and barriers for women to achieve their intended lifestyle changes were coded into categories based on the Behavioural Change Wheel framework (Michie et al 2011). Within this framework, the three factors of capability, opportunity and motivation, are considered to be key determinants of an individual's behaviour (Michie et al 2011). Capability refers to the individual's psychological and physical capacity to engage in the activity concerned, which includes having the necessary knowledge and skills (Michie et al 2011). Opportunity is defined as all the physical and social factors that make the behaviour possible or prompt it (Michie et al 2011). Motivation includes all those brain processes that direct behaviour, which includes habitual processes, emotional responding, and analytical decision-making (Michie et al 2011). Reporting of this study was based on the COREQ (consolidated criteria for reporting qualitative research) guideline (Tong et al 2007).

5.2.3 **Ethics**

This study received approval from the Children, Youth and Women's Health Service (CYWHS) Human Research Ethics Committee (REC 1860/8/12).

5.3 Results

5.3.1 **Participants**

During the study period, 25 eligible women were approached to join the qualitative study; of whom 22 women provided written informed consents and attended interviews and three women declined to participate. Two women declined to participate because they were too busy and one because of concern about her baby's health (Figure 5.1). Data saturation was reached within the sample size of 22 women.

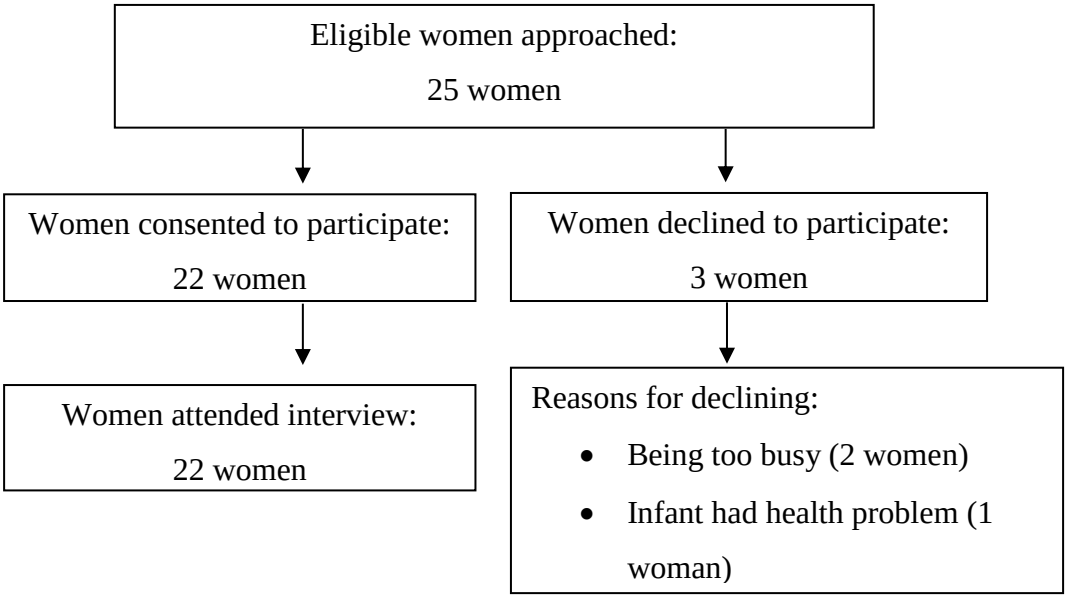


Figure 5.1 Flowchart of recruitment

Of the women who attended an interview, 10 (45.5%) were from the intervention group and 12 (54.5%) were from the control group. Over two thirds of interview participants were primiparous; two fifths of women were overweight or obese in early pregnancy; nearly half the women had a family history of diabetes mellitus, one woman had a medical history of hypertension and over two thirds of women had a socioeconomic status ranking of average or advantaged (Table 5.1). All women who attended for an interview reported they felt safe and relaxed during the interview.

Table 5.1 Characteristics of women approached for the study

Characteristics	Attended interview N=22		Declined interview N=3		Total N=25	
Maternal age (yr)[†]	30.3	6.0	31.3	12.5	30.4	6.7
Primiparity:	15	68.2	3	100.0	18	72.0
Ethnicity						
- **Caucasian**	13	59.1	3	100.0	16	64.0
- **Asian**	3	13.6	0		3	12.0
- **Other**	6	27.3	0		6	24.0
BMI at 1st visit (kg/m^2)[‡]	23.3	21.9, 29.3	20.9	20.2, 25.6	23.9	20.6, 28.8
BMI group[§]						
- **Underweight**	1	4.8	0		1	4.2
- **Normal**	11	52.4	2	66.7	13	54.2
- **Overweight**	4	19.0	1	33.3	5	20.8
- **Obesity**	5	22.8	0		5	20.8
Weight at 1st antenatal visit (kg) [†]	67.7	17.0	58.8	2.5	66.6	16.1
Smoker:	1	4.5	2	66.7	3	12.0
Mother history of hypertension:	1	4.5	0		1	4.0
Family history of hypertension[*]	6	27.3	0		6	24.0
Family history of DM[*]	10	45.5	0		10	40.0
Socioeconomic status[**]						
- **Most disadvantaged**	5	22.7	0		5	20.0
- **Disadvantaged**	1	4.6	0		1	4.0
- **Average**	7	31.8	0		7	28.0
- **Advantaged**	6	27.3	2	66.7	8	32.0
- **Most advantaged**	3	13.6	1	33.3	4	16.0

Figures are number and percentage.
[†]Mean and standard deviation; [‡]median and interquartile range; [§]weight and BMI at first antenatal visit were unknown for one woman who attended interview; underweight: BMI < 18.5 kg/m^2; normal: BMI 18.5-24.9kg/m^2; overweight: BMI 25.0-29.9 kg/m^2; obesity: BMI ≥30kg/m^2.
[*]Family history of hypertension and DM were unknown for one woman who did not attend interview.
[**]As measured by the Australian Bureau of Statistics (ABS) Socio-Economic Indexes for Areas (SEIFA) (ABS 2008).
BMI: body mass index; DM: diabetes mellitus

5.3.2 **Women's reactions to being diagnosed with borderline GDM**

Women showed a variety of reactions after being informed that they had borderline GDM (Table 5.2). Of the 14 women (64%) who reported that they were "not surprised", "not worried" or "felt ok" about the diagnosis, nine (64%) gave a reason for not being worried or surprised and five (36%) did not. Three (14%) reported they were not

Table 5.2 Women's experience after being told they had borderline GDM

Women's experience	Women	
	Number	%
Not surprised/ not worried/ felt ok	14	64
Mildly concerned/mildly worried	5	23
Scared/ worried/ concerned	3	13

surprised as they had a history of borderline GDM in previous pregnancies.

A further two (9%) women reported they were not surprised, as they had not been feeling well during pregnancy, which led them to expect the occurrence of GDM. One woman was not worried following an explanation about borderline GDM.

"Actually with my first daughter, I had the same problem, and that's you know, why I expected that my sugar level could be high with this one as well. So I wasn't quite surprised." (Woman 3)

Three (14%) women reported they were worried and/or had a feeling of failure after learning they had a positive OGCT. After being told their OGTT results, they were relieved or no longer felt worried.

"*Definitely felt surprised and a bit like a failure, that I had done something wrong. But, coming back as borderline gestational diabetes wasn't such an issue as having full-blown diabetes…and I don't worry about it*" (Woman 18)

Eight women (36%) reported being mildly worried or scared about having borderline GDM. The reasons they gave included being unsure about what caused the condition, about the health risks and about what was an appropriate diet to help reduce the health risks.

"When I know I [have] the borderline, actually I am scared. Because I always scared my baby will be too big, very hard to deliver, maybe we need to go to caesarean." (Woman 22)

5.3.3 **Women's attitudes towards managing their borderline GDM**

Almost all of the women (95%) rated managing their borderline GDM as important or very important whilst one woman (5%) was unsure. The most frequent reason given was that they believed management of bGDM could help with reducing their health risks or those of their babies.

5.3.4 **Information seeking and plans for diet and exercise**

When asked whether they had sought additional information about managing borderline GDM, 11 (50%) women reported they had, while the remaining 11 (50%) women did not. Sources they used included the internet (7 women), family members who had a history of type 2 diabetes mellitus (T2DM) or GDM (5 women) and health professionals (3 women). Four of these 11 women used more than one source for additional information.

For the 11 (50%) women who did not seek additional information, nine of them gave varied reasons that included already having received additional information via the IDEAL study (4 women), not being worried about borderline GDM (3 women), and no time to search for information (1 woman). Three women did not offer any reasons for not accessing information.

Thirteen women (59%) planned to improve both their diet and exercise pattern after learning of their borderline GDM diagnosis. Four women (18%) planned to improve diet only and one (5%) woman intended to improve exercise only as she felt her dietary

pattern was already appropriate. The remaining four women (18%) did not have any plans for changing their diet or exercise patterns, three of them because they felt these were already healthy.

5.3.5 The influence of family history of diabetes mellitus on women's feelings and experiences

Six of the 10 women who had a family history of diabetes mentioned this during their interview. Four women mentioned their family history of diabetes when asked about their feelings after knowing of their borderline GDM. Of these women, three reported they were mildly concerned and one woman reported she was not surprised. Two additional women mentioned their family history of diabetes when asked about information seeking and their plans for diet and lifestyle changes. The remaining four women did not mention their family history of diabetes mellitus during their interview.

5.3.6 Enablers and barriers for women to achieve intended diet and exercise changes

Enablers and barriers for women to achieve their intended lifestyle changes were classified under the three categories of "capability", "opportunity" and "motivation (Michie et al 2011). Six themes, including physical capability, psychological capability, physical opportunity, social opportunity, automatic motivation and reflective motivation, were used in our study (Table 5.3).

Table 5.3 Enablers and barriers for women to achieve their lifestyle goals

Enablers	Capability	Physical	- Physical fitness improved over time
		Psychological	- Knowing about healthy eating during pregnancy - Aware/ informed about bGDM/GDM
	Opportunity	Physical	- Active baby increases mother's activity - Baby easy to look after, allow more time for healthier lifestyle - Affordable childcare at gyms - Exercise sessions available on weekends - Allowed more time while on leave from work
		Social	- Support and/or encouragement from family members and friends
	Motivation	Automatic	- Used to healthy dietary pattern and/or active lifestyle - Craved healthier food - Likes exercise
		Reflective	- Cared about baby's health and/or own health - Wanted to lose weight or not gain too much weight - Tried to avoid food (e.g. sugar, soft drink) "causing" hyperglycaemia - Tried to set good examples for children at home - Thought about and planned diet and lifestyle goals in advance by using booklets from research study - Attended education sessions to discuss goals for diet and exercise - Wanted to make good value of the money paid for exercise sessions
Barriers	Capability	Physical	- Being tired, exhausted or having no energy - Experienced a painful pregnancy - Felt sick and nauseous or unwell - Low lying placenta - Had caesarean section - Had knee problem
		Psychological	- Unsure about proper diet and lifestyle for women with bGDM - Believed that pregnant women should not start exercising if not active before pregnancy
	Opportunity	Physical	- Being too busy - Lack of family support - Bad weather or getting dark early during winter - Having easy access to sugary food or chocolate

			- Changing in weather and environment while moving to another country - Shopping with young children is difficult - Having meals away from home
		Social	- The belief of "new mums could have chocolate, cakes or something sweet" - Lack of support from family members
	Motivation	Automatic	- Personal preference - Habits - Craved unhealthy food - Not motivated to exercise

GDM: gestational diabetes mellitus; bGDM: borderline gestational diabetes mellitus

5.3.6.1 ***Enablers***

Capability

With physical capability, improved physical health over time was raised as an enabler for both diet and exercise by women without prompting.

"…Because I felt better. I had a headache every single day for about a month, and as soon as I cut out a lot of the simple sugars the headaches went away and that was enough incentive to not ever, just not have any more." (Woman 1)

"*I've hired a cross-trainer; I just was waiting until I was all good down my caesarean… I go on there, a couple of, like, 5- or 10-minute bouts a day, just to do some sort of running exercise now.*" (Woman 6)

With psychological capability, enablers mentioned by women included having knowledge about healthy eating during pregnancy, receiving information about managing borderline GDM and gaining awareness about GDM. Sources for women to obtain relevant information included television, radio, magazines, family members and printed materials received through the IDEAL study.

"I suppose having information to start with, having these booklets (from the IDEAL study) *easy to read, and filling out your own plan, made you think about those things."* (Woman 15)

"I think just, awareness, sort of knowing what you have to do, like, you just don't want to do the wrong thing." (Woman 20)

Opportunity

Social and physical opportunities were identified under this category. The only social enabler mentioned was support and/or encouragement from family members and friends (eight women: 36%). Physical opportunities identified included the baby being active which offered more opportunity to move around, baby being easy to look after which allowed for more time, affordable childcare at gyms, exercise sessions available on weekends and being off work.

"I mean my parents are very much…into… encouraging, …we were brought up in an environment of … I would say healthy eating, …, like balanced eating, and being aware of low GI [glycaemic index] *and other things…"* (Woman 15)

Motivation

With automatic motivation, enablers highlighted included always maintaining a healthy diet and/or active lifestyle, craving for healthier food and liking exercise.

"Well, actually during the pregnancy itself I was just craving healthier food." (Woman 10)

With reflective motivation, care about baby's health and/or own health was one of the most frequently mentioned enabler, raised by 14 (78%) women. Other enablers

mentioned included wanting to lose weight or not gain too much weight (3 women), trying to avoid certain food (e.g. sugar, soft drink) which was thought to be the cause of hyperglycaemia (1 woman), trying to set good examples for children at home (1 woman), thinking about and planned diet and lifestyle goals in advance by using booklets from the IDEAL study (1 woman), attending education sessions to discuss about goals for diet and exercise (1 woman) and wanting to make good value of the money paid for exercise sessions (1 woman).

"Probably just prioritised, I don't want to put baby at risk of gestational diabetes, so you know, make sure I do what I need to do to keep her healthy." (Woman 17)

"I wanna try (to) *lose heaps more weight, cos after I had the other baby I put heaps of weight on, this time trying to lose like, heaps more and then try to, just, be fit."* (Woman 12)

5.3.6.2 ***Barriers***

Capability

With physical capability, seven women mentioned being "tired", "exhausted" or "no energy" as their barriers to achieving their intended diet and exercise goals. Tiredness was raised as a barrier by both antenatal women and postnatal women. For antenatal women, the tiredness was more frequently related to pregnancy itself, while postnatal women's tiredness was more likely to be a result of breastfeeding on demand and not having enough sleep. Other barriers reported by women included "experienced a painful pregnancy", "felt sick and nauseous", "low sitting placenta", "had caesarean section", "felt unwell" and "knee problem".

"...getting up with her during the night, I was very tired, and I'd kind of just ate a lot of sugar to give me energy." (Woman 9)

"Because I can't, like cook every day, it's very tiring; so basically, I normally will have (to) *go outside about 2-3 times a week. This is only main problem."* (Woman 22)

In terms of psychological capability, the barriers reported included being unsure about diet and exercise recommendations for women with borderline GDM and the belief that pregnant women should not start exercising if they were not active before pregnancy.

Opportunity

With physical opportunity, being too busy and/or lack of family support were the most frequently mentioned barriers (seven women). Other mentioned barriers were bad weather or getting dark early during winter, sugary food or chocolate being easily accessible, changing in climate and environment while moving to another country, shopping with kids and having meals away from home.

For social opportunity, the perception that new mums could have chocolate, cakes or something sweet and lack of support from family members were raised.

Motivation

Automatic motivation was the only theme identified under this category. The barriers mentioned included personal preference (two women: 9%), habits (two woman: 9%), pregnancy craving (one woman: 5%), and not well motivated (three woman: 14%).

"Maybe just like, I'm already fat or heavier after I give birth... Just leave it" (Woman 11).

"...you know just crave for something like that (chocolate)." (Woman 15)

5.3.7 **Women's needs to overcome barriers**

The needs expressed by women during their interviews varied considerably, depending on the barriers they experienced (Table 5.4). The most frequently mentioned needs were better family supports from partners and/ or parents. Two women reported nothing could help, as the barriers expressed by these two women were food craving and tiredness relating to pregnancy itself. Three of the four women who did not plan any changes to their diet or exercise also expressed their needs as being family support (two women), having information about nutrition and/ or management for borderline GDM (two women), overcoming depression (one woman), educating relatives and/ or friends about nutrition for pregnant women (one woman) and being able to organise their time better (one woman).

5.4 Discussion

From our qualitative semi-structured interview study, we find that a diagnosis of pregnancy hyperglycaemia without meeting GDM diagnostic criteria causes concerns to some women. Managing this mild form of pregnancy hyperglycaemia is perceived by women as important, although most women do not seek out information by themselves. Women are willing to improve their lifestyle but achieving a successful lifestyle modification is influenced by a wide range of factors. Thinking about baby's health and their own health was highlighted as one of the most important facilitators to achieve a healthier lifestyle. On the other hand, being physically unwell, having a busy life, and not having adequate family support were the most frequently mentioned inhibitors. Women with pregnancy hyperglycaemia express many different needs, the most common being need for better family support and receiving appropriate diet and exercise information.

Table 5.4 Summary of needs raised by women to help with overcoming barriers

Needs	Number of women
Family support from partner and/ or parents	5
Diet and exercise information for pregnant women/ bGDM	4
Being off work	3
Having diet and/exercise sessions with health professional	3
Better weather for exercise	2
Educate relatives and/ or friends about nutrition during pregnancy	2
Baby sleeps through night/ becomes easier to be looked after	2
Access to pre-prepared healthy food	2
Make own decision on what to eat	1
Access to flexible time childcare	1
Return to normal health after childbirth	1
Help from health professionals to get more motivated	1
Nothing could help	2

bGDM: borderline gestational diabetes mellitus.

Previous qualitative studies using a semi-structured or in-depth interview method have been undertaken to examine women's experiences and attitudes after being diagnosed with GDM and the facilitators and inhibitors to the intended lifestyle management (Bandyopadhyay et al 2011; Carolan 2013; Carolan et al 2012; Evans and O'Brien 2005; Hjelm et al 2012; Hjelm et al 2005; Hjelm et al 2008; Trutnovsky et al 2012). However, there are limited data on women's experiences after being diagnosed with pregnancy hyperglycaemia without meeting GDM diagnostic criteria and little is known about the enablers and barriers for them to achieve healthier lifestyles.

Findings from qualitative studies targeting women with GDM (meeting GDM diagnostic criteria) (Bandyopadhyay et al 2011; Carolan 2013; Carolan et al 2012; Evans and O'Brien 2005; Hjelm et al 2012; Hjelm et al 2005; Hjelm et al 2008;

Trutnovsky et al 2012) provide a context for our results although their research populations are different from those of the current study in terms of a greater degree of pregnancy hyperglycaemia.

In contrast with our results, negative feelings such as being upset, fear, shock or worries after the diagnosis of GDM were more frequently mentioned in previous studies investigating the experience of women with GDM (Bandyopadhyay et al 2011; Carolan 2013; Hjelm et al 2012; Hjelm et al 2005; Hjelm et al 2008; Trutnovsky et al 2012).

Consistent with our results, concerns about baby's health was found as a main motivational factor for women seeking GDM management (Carolan et al 2012; Evans and O'Brien 2005; Hjelm et al 2005; Trutnovsky et al 2012) and more information about lifestyle management after diagnosis was wanted (Hjelm et al 2008).

Time pressures, physical constraints and lack of clear guidelines were the main barriers to achieving lifestyle self-management. Facilitators in other studies were thinking about the baby and having support from family members in women with GDM from low socio-economic and migrant backgrounds living in Australia (Carolan et al 2012). These findings are similar to our study results. Amongst 17 immigrant women from South Asia with GDM living in Australia, the need for culturally appropriate dietary advice was found (Bandyopadhyay et al 2011). This was not apparent in our study.

Our study is the first qualitative semi-interview study targeting women with borderline GDM. It helps provide an in-depth understanding of women's views and perceptions towards the diagnosis and management of borderline GDM, as well as providing information about important factors that affect women's ability to achieve their intended lifestyle modifications. Therefore, the findings of our study may help with designing and delivering tailored care for women with mild pregnancy hyperglycaemia in the

future. A limitation to our study is that only women who could speak English were eligible, so women from different cultural backgrounds may have been excluded. Inclusion of non-English speaking women from different ethnic groups may be worth considering in future studies, given our culturally diverse community in Australia.

Our findings are based on information provided by women from one geographical area, which may have limited generalisability to pregnant populations. As the interviewer was a dietitian, this may have influenced women's responses. To overcome this, efforts were made by assuring women that the interviewer was primarily a researcher and interviews were conducted away from the clinic area.

5.5 Conclusion

This study shows the diagnosis of borderline GDM can cause worries for some women although lifestyle management was identified as important by most women affected. Factors impacting women's ability to achieve intended lifestyle changes vary greatly, with the most important enabler as thinking about baby's health and the most significant barrier being a lack of family support.

6 The In-depth IDEAL 4 to 12 month Follow-Up Study - maternal and infant health outcomes after receiving diet and exercise advise during pregnancy or routine care for managing borderline gestational diabetes mellitus

6.1 Introduction

Large trials with sufficient power to assess short- and longer-term effects of lifestyle interventions for women with pregnancy hyperglycaemia without meeting GDM diagnostic criteria are clearly needed as outlined in the research recommendation from the Cochrane systematic review presented in Chapter 4 of this thesis. One such trial, the IDEAL Trial of "investigation of dietary advice and lifestyle for women with borderline gestational diabetes: a randomised controlled trial," has recently completed recruitment (Crowther et al 2012). Maternal and infant outcomes at birth and during the early postnatal period will be reported in the main IDEAL Trial report (Crowther et al 2012). This chapter reports the findings from the women and babies who are able to participate in the In-depth IDEAL 4 to 12 month Follow-Up Study as part of this thesis.

The candidate (Shanshan Han) designed the study, wrote the study protocol, planned analyses and interpreted research findings; has been involved in recruiting eligible women and their babies, conducting follow-up assessments and coordinating interstate participating centre for the Follow-Up Study.

6.2 Study aims and hypotheses for the In-depth IDEAL 4 to 12 month Follow-Up Study

The aim of the In-depth IDEAL 4 to 12 month Follow-Up Study was to assess the health related outcomes of the women and their babies enrolled in the IDEAL Trial at 4 to 12 months after birth. Women and their babies allocated at randomisation to the intervention group were compared with those in the routine care group. Infant growth, maternal postpartum weight retention, and their body fat distribution were assessed during the follow-up assessment.

The primary hypotheses were that additional care (diet and exercise advice, with regular monitoring of blood glucose concentrations during pregnancy) for managing borderline GDM compared with routine care would:

1) Significantly increase the number of infants with a healthy body weight (defined as infant weight within the range of 10^{th} to 90^{th} centile on WHO 2006 growth charts (WHO 2006)) at four to twelve months of age.
2) Significantly increase the number of women returning to their prepregnancy weight at four months postpartum.

The secondary study hypotheses were that additional care for women with borderline GDM during pregnancy compared with routine care would:

1) Reduce infant subcutaneous adiposity at follow up as assessed by skinfold thickness at follow-up.
2) Reduce maternal subcutaneous adiposity at follow up as assessed by skinfold thickness at follow-up.

6.3 Methods

6.3.1 Participants eligible for the In-depth IDEAL 4 to 12 month Follow-Up Study

All women and their babies enrolled in the IDEAL Trial at Women's and Children's Hospital (WCH), Adelaide, South Australia, Lyell McEwin Hospital, Adelaide, South Australia, Flinders Medical Centre, Adelaide, South Australia and Royal Women's Hospital, Melbourne, Victoria, who were within the 12 months postpartum period from February 2011 and April 2013, were eligible and invited to participate in this Follow-Up Study.

6.3.2 The IDEAL Trial: summary of research methods

The methods of the IDEAL randomised controlled trial, previously published elsewhere, are summarised below (Crowther et al 2012).

6.3.2.1 Eligibility criteria for the IDEAL Trial

Women between 24^0 and 34^6 weeks gestation with a singleton pregnancy, a positive oral 50 gram glucose challenge test (OGCT) (venous plasma glucose >7.8 mmol/L) and a normal oral 75 gram glucose tolerance test (OGTT) (fasting venous plasma glucose <5.5 mmol/L and a 2 hour glucose <7.8 mmol/L), who gave written, informed consent.

6.3.2.2 Exclusion criteria for the IDEAL Trial

Women with known diabetes mellitus, previously treated GDM, active chronic systemic disease (except essential hypertension and mild forms of asthma) or a multiple pregnancy.

6.3.2.3 Trial entry and randomisation

Eligible women were offered the study information sheet, counselled prior to their OGTT, and entered into the trial if they had a normal OGTT result and gave consent. Group allocation was based on a central telephone randomisation service using a randomisation schedule with balanced variable blocks, prepared by an investigator not involved with recruitment or clinical care.

6.3.2.4 The IDEAL Trial study groups and interventions

Women in the 'Intervention Group' were advised that their oral glucose tolerance test results were normal but that they had borderline glucose intolerance. They received antenatal care from the attending medical team, which included diet and exercise advice, monitoring of blood glucose concentrations and further treatment if appropriate.

Diet and exercise advice: Women had individualised advice regarding their diet from a qualified dietitian, based on current available recommendations including the Australian Guide to Healthy Eating (Kellett et al 1998) and online resources produced by the Dietitians Association of Australia, the Women's and Children's Hospital and Diabetes SA. Moderate exercise was recommended as an adjunct to dietary intervention (Gillies et al 2007; Hoffman et al 1998). Written information was given to the women and a pregnancy record booklet was provided for them to review their diet and exercise, and set goals at monthly intervals after an initial counselling session with a dietitian.

Blood glucose assessments: After trial entry, women had their blood glucose monitored at each antenatal visit with a single, capillary blood glucose test (either fasting or 1 or 2 hours postprandial).

Further antenatal care: Women attended routine antenatal visits according to standard practice for each hospital. At each visit, progress with their dietary and exercise goals was reviewed with their health professionals and this was recorded in their antenatal study booklet. Care of women otherwise followed routine clinical practice.

Women in the 'Routine-care Group' were advised that their oral glucose tolerance test results were normal. They received routine antenatal care according to current clinical practice in hospitals in Australia for women who had a positive OGCT result but normal OGTT results (Crowther et al 2012).

The main IDEAL Trial has recently completed recruitment and results from the study are pending at the time of submitting this thesis.

6.3.3 Contact with the families and recruitment procedures for the In-depth IDEAL 4 to 12 month Follow-Up Study

During the antenatal and early postnatal periods (before 4 months postpartum), a variety of strategies were used to encourage a high follow-up rate. These included obtaining additional contact details for contact person (s) at entry into the IDEAL Trial, mailing regular newsletters about the progress of the study to women, specifically checking with the women for any change of contact details, and providing a fridge magnet with printed reminders for women to contact IDEAL Trial coordinating centre for any change of contact details. A freepost service was provided for families to post their updated contact details. Any changes in contact details received were updated on the IDEAL Trial database so that subsequent tracing of families was facilitated.

The In-depth IDEAL Follow-Up Study commenced recruitment in February 2011. Families were contacted when their babies were three and half months or older. Phone calls at different time points of the day were made by the candidate in South Australia

and by the research assistant in Melbourne if no contact was made at the first attempt. Contacting mothers during their postnatal hospital visit (if a visit occurred), was also planned if phone calls had not yet been successful in making contact.

If parents consented to participate in the follow up study but were not able to attend the assessment when their babies were 4 months old, arrangements were made for follow up when their babies were around 6, 8, or 12 months old where possible, until a visit was made.

6.3.4 Data collection and assessments made at the In-depth IDEAL 4 to 12 month Follow-Up Study

Information on maternal pre-pregnancy or early pregnancy weight (weight at first antenatal appointment) and socio-demographic characteristics was abstracted from hospital records and maternal questionnaires from the IDEAL Trial.

6.3.4.1 Maternal assessment

At the follow-up assessment, maternal weight, height, waist circumference and gluteal circumference were measured. Four maternal sites (biceps, triceps, suprailiac area and subscapular) skinfold thicknesses were measured during the visit according to standard anthropometric assessment methods (Marfell-Jones et al 2006). All skinfold thickness measurements were taken on the right side of the body. Two measurements were done at each specified site and the average of the two measurements was used for data analysis. If results differed by more than 7.5% between the two measurements, a third measure was done. The average of the two closest readings was used in the data analysis.

6.3.4.2 Infant assessment

At the follow-up assessment, infants' weight, length, head circumference, arm circumference, chest circumference and abdominal circumference were measured. The most recent World Health Organization (WHO) child growth standards were used to assess the infants' growth in terms of weight-for-age, length-for-age, head circumference-for-age (WHO 2006; 2007). A z-score, which indicates how many standard deviations a value is from the mean, for infant weight, length and head circumference at different ages, were obtained from the WHO child growth standards (WHO 2006; 2007).

The infants' subcutaneous adiposity was assessed by skinfold thickness (Schmelzle and Fusch 2002). Standard anthropometric assessment methods were used (Marfell-Jones et al 2006). Where possible, two skin-fold measurements were taken at every specified site and the average of the two measurements was used in the data analysis. If results differed by more than 7.5% between the two measurements, a third measure was performed. The average of the two closest readings was used in data analysis.
Staff involved in outcome data abstraction and follow up assessment were blinded to treatment group allocation. Follow-up assessments were conducted by research staff with appropriate training. All information collected was kept strictly confidential and kept in locked filing cabinets. Outcome assessors and investigators, including the candidate were all blinded to treatment groups until data analyses were completed.

6.3.5 **Study outcomes for the In-depth IDEAL 4 to 12 month Follow-Up Study**

Primary outcomes:

1. Infant weight z-score at follow up: calculated by subtracting the population mean from the raw score for infant weight and then dividing the difference by

the population standard deviation. Population mean and standard deviation were based on WHO child growth standards (WHO 2006).

2. The incidence of women within 1 kg of their prepregnancy or early pregnancy weight by four-months postpartum.

Secondary outcomes:

1. The incidence of infants' weight above 90th centile based on WHO 2006 growth standards (WHO 2006).
2. The incidence of infants' weight below 10th centile based on WHO 2006 growth standards (WHO 2006).
3. Infant length z-score at follow-up: calculated by subtracting the population mean from the raw score for infant length and then dividing the difference by the population standard deviation. Population mean and standard deviation were based on WHO child growth standards (WHO 2006).
4. Infant head circumference z-score at follow-up: calculated by subtracting the population mean from the raw score for infant head circumference and then dividing the difference by the population standard deviation. Population mean and standard deviation were based on WHO child growth standards (WHO 2007).
5. Infant ponderal index at four months of age: calculated by weight in kilograms divided by the third power of body height in metres (weight (kg)/ height^3 (m)).
6. Infant chest circumference at four months of age.
7. Infant arm circumference at four months of age.
8. Infant abdominal circumference at four months of age.

9. Infant subcutaneous adiposity as measured by skinfold thickness: measured at biceps, triceps, abdomen, suprailiac area, subscapular and thigh (Nevill et al 2006; Schmelzle and Fusch 2002; Wells and Fewtrell 2006).
10. Infant central subcutaneous adiposity at four months of age: defined as a sum of suprailiac and subscapular skinfold thickness (Birmingham et al 1993; Ketel et al 2007).
11. Infant peripheral subcutaneous adiposity at four months of age: defined as a sum of triceps and biceps skinfold thickness (Birmingham et al 1993; Ketel et al 2007).
12. Infant total subcutaneous adiposity at four months of age: defined as a sum of suprailiac, subscapular, triceps and biceps skinfold thickness (Birmingham et al 1993; Ketel et al 2007).
13. Infant central-to-peripheral subcutaneous fat distribution at four months of age: defined as subscapular-to-triceps ratio (Haffner et al 1987).
14. Infant central-to-total subcutaneous fat distribution at four months of age: defined as percentage of central subcutaneous adiposity to total subcutaneous adiposity ((subscapular skinfold thickness + suprailiac skinfold thickness) ÷ (sum of suprailiac, subscapular, triceps and biceps skinfold thickness) ×100) (Weststrate et al 1989).
15. Incidence of women with excessive weight retention: weight ≥ 4.5kg above their prepregnancy or early pregnancy weight at four months after birth.
16. Maternal BMI at four months postpartum.
17. Maternal BMI category at four months postpartum: underweight (BMI <18.5kg/m^2), normal weight (BMI 18.5 kg/m^2 to 24.9 kg/m^2), overweight (BMI 25-29.9kg/m^2) and obese (BMI ≥30kg/m^2).
18. Maternal arm circumferences at four months postpartum.

19. Maternal waist circumference at four months postpartum.
20. Maternal gluteal circumferences at four months postpartum.
21. Maternal subcutaneous adiposity as measured by skinfold thickness at four months postpartum: skinfolds thickness measured at biceps, triceps, suprailiac area and subscapular) (Birmingham et al 1993; Ketel et al 2007).
22. Maternal central subcutaneous adiposity at four months postpartum: defined as a sum of suprailiac and subscapular skinfold thickness (Birmingham et al 1993; Ketel et al 2007).
23. Maternal peripheral subcutaneous adiposity at four months postpartum: defined as a sum of triceps and biceps skinfold thickness (Birmingham et al 1993; Ketel et al 2007).
24. Maternal total subcutaneous adiposity at four months postpartum: defined as a sum of suprailiac, subscapular, triceps and biceps skinfold thickness (Birmingham et al 1993; Ketel et al 2007).
25. Maternal central-to-peripheral subcutaneous fat distribution at four months postpartum: defined as subscapular-to-triceps ratio (Haffner et al 1987).
26. Maternal central-to-total subcutaneous fat distribution at four months of age: defined as percentage of central subcutaneous adiposity to total subcutaneous adiposity ((subscapular skinfold thickness + suprailiac skinfold thickness) ÷ (sum of suprailiac, subscapular, triceps and biceps skinfold thickness) ×100) (Weststrate et al 1989).

6.3.6 **Sample size for the In-depth IDEAL 4 to 12 month Follow-Up Study**

Infant weight z-score at 4 to12 months of age was the primary endpoint of the In-depth IDEAL Follow-Up Study. A total of 210 infants was calculated to be able to detect a change in mean z-score between the treatment groups of 0.4 (two-tailed alpha=0.05, 80% power, 5% loss to follow up).

The incidence of women within 1 kg of their prepregnancy weight at four months postpartum was the primary maternal outcome. A study from the US found that 52% women in the group receiving diet and exercise intervention were not within 1 kg of their pregnancy weight by 16 weeks postpartum compared with 79% women in the group continuing their usual diet and lifestyle, a 34% relative risk difference (Lovelady et al 2000). A trial of 145 women would be able to show a more conservative reduction in the relative risk of retaining more than 1 kg weight at four months postpartum of 30% from 79% to 55% with lifestyle intervention (5% level of significance, two-tailed alpha, 80% power, 5% loss to follow up).

6.3.7 **Statistical analyses**

The initial analyses were carried out to assess women's baseline demographic and pregnancy information at the time of entry to the IDEAL Trial. This baseline descriptive analysis was performed to compare the characteristics of women involved the In-depth Follow-up Study with women in the main IDEAL Trial; and the characteristics of women participated in the In-depth Follow-Up Study compared between intervention group and routine-care group. Means and standard deviations, or medians and interquartile ranges were reported for continuous variables where appropriate. Frequencies and percentages were reported for categorical variables.

All subsequent analyses were based on intention-to-treat approach in which all participants were analysed according to their treatment allocation at randomisation. Both unadjusted and adjusted analyses were performed for all primary and secondary outcome variables. Baseline predictors with substantial imbalance identified in subsequent analyses including maternal smoking status, ethnicity, and family history of diabetes were controlled for in adjusted analyses. Randomisation stratification factors for the IDEAL Trial including collaborating centres and OGCT results and potential

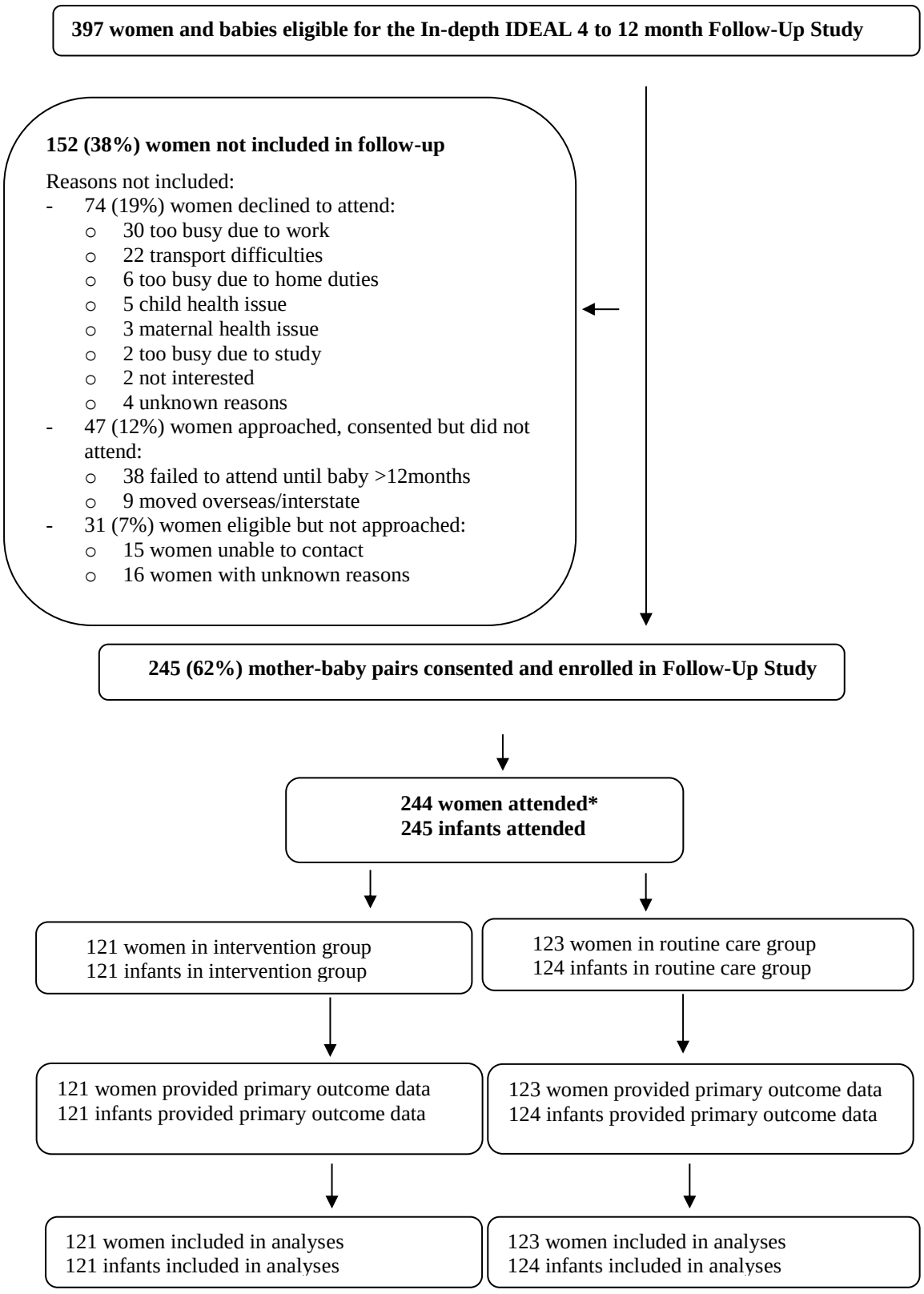


Figure 6.1 Study flowchart for the In-depth IDEAL 4 to 12 month Follow-Up Study

*baby and father attended, but not mother

confounders including maternal BMI at first antenatal appointment, socio-economic status, maternal age, parity and gestational age at IDEAL trial entry were also additionally controlled for in a further set of adjusted analyses.

Binary outcomes were analysed using log binomial regression, with treatment effects expressed as relative risks (RR) with 95% confidence intervals (CI), or a Fisher's exact test with no adjustment for baseline covariates in the case of rare outcomes. Effect of treatment groups on continuous outcomes were presented as differences in means with 95% CI using linear regression.

Ordinal outcomes were analysed using proportional odds models, with treatment effects expressed as odds ratios of higher severity. The WHO 2006 growth reference (WHO 2006; 2007) was used to determine age and sex-specific percentiles and z-scores for weight, length and head circumference of the infants at 4 months of age.

Statistical significance was assessed at the 0.05 level using a two-sided comparative test of treatment effect, comparing the intervention group to the routine-care group. No adjustment was made for multiple comparisons and clustering of women in the same centre. All analyses were performed using SAS® software version 9.3 (SAS Institute Inc., Cary, NC, USA).

6.4 Results

6.4.1 **Recruitment and flow of participants**

The flow of eligible women approached, those declining and their reasons and the numbers of women and babies who were able to provide primary outcome data for the In-depth IDEAL 4 to 12 month Follow-Up Study are listed in Figure 6.1.

Table 6.1 Maternal baseline characteristics for the Follow-Up Study cohort and the IDEAL Trial cohort

Maternal baseline characteristics	Follow-Up Study N=245		IDEAL Trial N=724	
Maternal age (year)[†]	31.4	4.9	30.6	5.1
Gestational age at trial entry (week)[†]	30.5	1.9	30.3	1.9
Primiparity	139	56.7	382	52.8
Weight at 1st antenatal visit[‡] **(kg)**	65.0	59.0, 75.0	65.4	59.0, 78.0
BMI at 1st antenatal visit[‡] **(kg/m^2)**	24.2	21.9, 27.8	24.6	22.0, 28.3
BMI category at 1st antenatal visit				
- **Underweight (<18.5 kg/m^2)**	6	2.4	16	2.3
- **Normal (18.5-24.9 kg/m^2)**	136	55.5	358	51.6
- **Overweight (25-29.9 kg/m^2)**	61	24.9	184	26.5
- **Obese (≥30 kg/m^2)**	42	17.1	136	19.6
OGCT result[‡] **(mmol/L)**	8.5	8.1, 9.0	8.5	8.1, 9.1
OGTT Fasting result (mmol/L)[†]	4.4	0.4	4.4	0.4
OGTT 2 hour result (mmol/L)[†]	6.2	1.0	6.2	1.1
Previous pregnancy ≥20 weeks	106	43.3	342	47.2
Obstetric history[§]				
- **Preterm birth**	8	7.5	33	9.6
- **Fetal trauma**	1	0.9	3	0.9
- **Pre-eclampsia**	3	2.8	14	4.1
- **Shoulder dystocia**	3	2.8	8	2.3
- **Caesarean section**	34	32.1	96	28.1
- **Perinatal death**	6	5.7	14	4.1
Maternal history of hypertension	14	5.7	40	5.6
Family history of diabetes	91	37.6	261	36.5
Family history of hypertension	96	39.8	277	38.8
Ethnicity				
- **Caucasian**	164	66.9	522	72.1
- **Asian**	59	24.1	138	19.1
- **Other**	22	9.0	64	8.8
Smoking at entry[*]	24	10.0	106	15.0
Socioeconomic status[**]				
- **Most disadvantaged**	57	23.3	157	21.7
- **Disadvantaged**	44	18.0	112	15.5
- **Average**	46	18.8	142	19.6
- **Advantaged**	53	21.6	173	23.9
- **Most advantaged**	45	18.4	140	19.3

Figures are numbers and percentage; [†]mean and standard deviation; [‡]median and interquartile range;
[§]among women with previous pregnancies at ≥20 weeks;
[*]smoking status was unknown for two women in the intervention group and two women in the control group;
[**] as measured by the Australian Bureau of Statistics (ABS) Socio-Economic Indexes for Areas (SEIFA) (ABS 2008).
BMI: body mass index

Over the recruitment period (February 2011 to April 2013), 397 women and babies were eligible for the study. Of these, 245 (62%) mother-baby pairs consented and enrolled the In-depth Follow-Up Study. The largest proportion of women (n=165, 67%) were recruited from the South Australian sites (Women's and Children's Hospital (WCH) (n=110, 45%), Lyell McEwin Hospital (n=22, 9%) and Flinders Medical Centre (n=33, 13%), and 80 (33%) women were recruited from the Royal Women's Hospital in Melbourne, Victoria. Primary outcome data were available for 244 (99.6%) women and 245 (100%) babies. One baby and father attended the four-month follow-up but as the mother was unable to attend her data were unable to be included in these analyses.

Of the 152 (38%) eligible women and their babies not included in the Follow-Up Study, 74 (19%) declined participation, 47 (12%) consented to the Follow-Up Study but failed to attend the assessment and 31 (7%) were not able to be approached. Detailed reasons for non-attendance or not being approached are listed in Figure 6.1.

6.4.2 **Maternal baseline characteristics**

At trial entry into the IDEAL Trial, baseline characteristics were similar between women involved in the In-depth IDEAL 4 to 12 month Follow-Up Study and those in the IDEAL main trial (Table 6.1).

Of the 245 mother and baby pairs enrolled in the Follow-Up Study, 121 (49%) were randomised to the intervention group and 124 (51%) to the routine-care group. Baseline characteristics, including maternal age, gestational age at trial entry, primiparity, weight and body mass index (BMI) at first antenatal appointment, oral glucose challenge test (OGCT) results, oral glucose tolerance test (OGTT) results, maternal medical history of hypertension, and family history of hypertension, were similar between women from the two study groups at trial entry into the IDEAL Trial (Table 6.2). In a subset of women

Table 6.2 Baseline characteristics of women enrolled in the Follow-Up Study by treatment group

Characteristics	Intervention group N= 121		Routine-care group N=124	
Maternal age (yr)[†]	31.4	5.0	31.3	4.8
Gestational age at trial entry (wk)[†]	30.2	2.0	30.7	1.9
Primiparity	71	58.7	68	54.8
Weight at 1st antenatal visit[‡] **(kg)**	65.0	59.0, 79.1	65.2	58.5, 72.7
BMI at 1st antenatal visit[‡] **(kg/m^2)**	24.2	22.0, 29.0	24.2	21.8, 27.2
BMI category at 1st antenatal visit				
- **Underweight (<18.5 kg/m^2)**	4	3.3	2	1.6
- **Normal (18.5-24.9 kg/m^2)**	65	53.7	71	57.3
- **Overweight (25-29.9 kg/m^2)**	26	21.5	35	28.2
- **Obese (≥30 kg/m^2)**	26	21.5	16	12.9
OGCT result[‡] **(mmol/L)**	8.6	8.1, 9.1	8.4	8.1, 8.9
OGTT Fasting result (mmol/L)[†]	4.3	0.4	4.4	0.4
OGTT 2 hour result (mmol/L)[†]	6.2	1.0	6.2	1.0
Previous pregnancy ≥20 wks	50	41.3	56	45.2
Obstetric history[§]				
- **Preterm birth**	3	6.0	5	8.9
- **Fetal trauma**	0	0.0	1	1.8
- **Pre-eclampsia**	2	4.0	1	1.8
- **Shoulder dystocia**	2	4.0	1	1.8
- **Caesarean section**	19	38.0	15	26.8
- **Perinatal death**	1	2.0	5	8.9
Maternal history of hypertension	8	6.6	6	4.8
Family history of diabetes	59	49.2	32	26.2
Family history of hypertension	47	39.5	49	40.2
Ethnicity				
- **Caucasian**	89	73.6	75	60.5
- **Asian**	23	19.0	36	29.0
- **Other**	9	7.4	13	10.5
Smoking at entry[*]	17	14.1	7	5.7
Socioeconomic status[**]				
- **Most disadvantaged**	29	24.0	28	22.6
- **Disadvantaged**	18	14.9	26	21.0
- **Average**	23	19.0	23	18.6
- **Advantaged**	29	24.0	24	19.4
- **Most advantaged**	22	18.2	23	18.6

Figures are numbers and percentage;
[†]mean and standard deviation;
[‡]median and interquartile range.
[§]Among women with previous pregnancies at ≥20 weeks.
[*]Smoking status was unknown for two women in the intervention group and two women in the control group.
[**]As measured by the Australian Bureau of Statistics (ABS) Socio-Economic Indexes for Areas (SEIFA) (ABS 2008).
BMI: body mass index

with one or more previous pregnancies 20 weeks or more, obstetric baseline characteristics including preterm birth, fetal trauma, pre-eclampsia, shoulder dystocia were similar between the two study groups (Table 6.2). For some characteristics, differences between the two treatment groups were seen. A higher proportion of women in the intervention group when compared with those in the routine-care group were obese at first antenatal visit (21.5% versus 12.9%), had a family history of diabetes (49.2% versus 26.2%), were Caucasian (73.6% versus 60.5%) and smoked at trial entry (14.1% versus 5.7%) (Table 6.2). Compared with women in the routine-care group, a lower proportion of women in the intervention group were Asian (19.0% versus 29.0%) (Table 6.2). Women in the intervention group had a higher socioeconomic status rating when compared with women in the routine-care group, where 24.0% women in the intervention group were rated as advantaged versus 19.4% in the routine-care group and 14.9% women in the intervention group were rated as disadvantaged versus 21.0% in the routine-care group (Table 6.2). Among women with a history of previous pregnancies at 20 weeks or more, women in the intervention group were more likely to have a history of caesarean section when compared with women in the routine-care group (38.0% versus 26.8%) and less likely to have a history of perinatal death (2.0% versus 8.9%) (Table 6.2).

6.4.3 **Primary outcomes**

6.4.3.1 Infant outcomes

Infants born to women in the intervention group compared with those born to women in the routine-care group did not have a statistically significant difference in weight z-score (245 infants, 0.24 versus 0.36, mean difference (MD) -0.13, 95% confidence interval (CI) -0.38 to 0.12, unadjusted p= 0.32) (Table 6.3). When adjusted for baseline imbalances for maternal BMI at first antenatal visit, smoking status, ethnicity, family

Table 6.3 Infant anthropometric outcomes based on WHO 2006 growth standards at follow-up by treatment group

Outcomes	Intervention group N= 121		Routine-care group N= 124		Unadjusted effect (95%CI)		P-value	Adjusted effect* (95%CI)		P-value*	Adjusted effect** (95%CI)		P-value**
Weight z-score†	0.24	1.0	0.36	1.0	-0.13	-0.38, 0.12	0.32	-0.06	-0.32, 0.19	0.63	-0.05	-0.31, 0.20	0.68
Length z-score	0.65	1.1	0.85	1.1	-0.19	-0.46, 0.08	0.16	-0.07	-0.34, 0.20	0.61	-0.09	-0.36, 0.18	0.52
Head circumference z-score	0.83	1.1	0.83	1.1	0.00	-0.27, 0.27	1.00	0.02	-0.26, 0.30	0.88	0.08	-0.20, 0.35	0.59
Weight> 90th centile‡	19	15.7	20	16.1	0.97	0.55, 1.73	0.93	1.18	0.66, 2.13	0.58	1.23	0.69, 2.19	0.49
Weight< 10th centile‡	10	8.3	5	4.0	2.05	0.72, 5.82	0.18	NA		NA	NA		NA

Values are means (standard deviation), and effects are mean difference (95% confidence interval) unless otherwise indicated.

‡Values are numbers (%), and treatment effects are relative risks (95% confidence interval).

†Primary outcome.

*Adjusted for baseline imbalances: in maternal BMI at first antenatal visit, smoking status, ethnicity, family history of diabetes and socioeconomic status.

**Adjusted for baseline imbalances and potential confounders: maternal BMI at first antenatal visit, smoking status, ethnicity, family history of diabetes, socioeconomic status, centres, oral glucose challenge test result, gestational age at entry, age and parity.

NA: not applicable as there were too few outcome events for adjusted analysis.

history of diabetes, socioeconomic status, and for baseline imbalances plus the potential confounders of recruitment centre, maternal age, parity, OGCT results and gestational age at IDEAL trial entry, the differences remained non-significant (Table 6.3).

6.4.3.2 Maternal outcomes

The incidence of women within 1 kg of their prepregnancy or early pregnancy weight by four months postpartum was 11.6% (n=8) for women in the intervention group and 15.7% (n=11) for women in the routine-care group (Table 6.4). The difference between the two study groups was not statistically significant in the unadjusted analysis (139 women, relative risk (RR) 0.74, 95% CI 0.32 to 1.72, p=0.48) or in either adjusted analyses (Table 6.4).

6.4.4 **Secondary outcomes**

6.4.4.1 Infant outcomes

There was no significant difference between the two study groups in the proportion of infants with weight above the 90th centile based on the WHO 2006 growth standards at follow-up in the unadjusted analysis (245 infants, RR 0.97, 95% CI 0.55 to 1.73, unadjusted p= 0.93) or the adjusted analyses (Table 6.3). Infants born to women in the intervention group were not more likely to have a weight below the 10th centile on the WHO 2006 growth standards when compared with those born to women in the routine-care group at 4 to 12 month follow-up (245 infants, RR 2.05, 95% CI 0.72 to 5.82, unadjusted p=0.18) (Table 6.3).

At follow-up, there was no significant difference between the two study groups in infant length z-score in the unadjusted analysis (245 infants, MD -0.19, 95% CI -0.46 to 0.08, unadjusted p=0.16) or the adjusted analyses (Table 6.3). Similarly no significant

Table 6.4 Maternal anthropometric outcomes at four months postpartum by treatment group

Outcomes	Intervention N= 69		Routine-care N= 70		Unadjusted effect (95%CI)		P-value	Adjusted effect* (95%CI)		P-value*	Adjusted effect** (95%CI)		P-value**
Weight within 1kg of prepregnancy or early pregnancy weight[†]	8/69	11.6	11/70	15.7	0.74	0.32, 1.72	0.48	0.70	0.29, 1.68	0.42	0.75	0.31, 1.82	0.53
Weight ≥4.5kg of prepregnancy or early pregnancy weight	31/69	44.9	33/70	47.1	0.95	0.66, 1.37	0.79	NA		NA	NA		NA
Weight change between 4 months postpartum and trial entry (kg)[‡]	1.7	5.7	1.7	5.8	-0.02	-1.93, 1.89	0.98	0.05	-2.01, 2.11	0.96	-3.0	-2.37, 1.78	0.78
Maternal BMI (kg/m^2)[‡]	27.0	5.6	25.7	4.1	1.33	-0.30, 2.95	0.11	0.67	-0.29, 1.63	0.17	0.55	-0.41, 1.50	0.26
BMI change between 4 month postpartum and trial entry (kg/m^2)[‡]	1.0	2.2	1.1	2.4	-0.09	-0.84, 0.75	0.81	-0.04	-0.84, 0.75	0.92	-0.16	-0.97, 0.64	0.69
BMI categories[§]					1.58	0.84, 2.95	0.15	1.52	0.62, 3.69	0.36	1.22	0.48, 3.14	0.68
- **Underweight (< 18.5 kg/m^2)**	2/69	2.9	0/70	0.0									
- **Normal weight (18.5-24.9 kg/m^2)**	29/69	42.0	38/70	54.3									
- **Overweight (25-29.9 kg/m^2)**	16/69	23.2	20/70	28.6									
- **Obese (≥ 30 kg/m^2)**	22/69	31.9	12/70	17.1									
Circumference (cm)[‡]													
- **Arm**	29.5	4.9	29.5	3.8	0.00	-1.44, 1.44	1.00	-0.40	-1.58, 0.79	0.51	-0.18	-1.35, 1.00	0.77
- **Gluteal**	103.7	11.2	101.6	9.3	2.05	-1.34, 5.45	0.24	0.43	-1.96, 2.82	0.72	0.08	-2.36, 2.51	0.95
- **Waist**	82.0	11.6	79.0	9.4	2.98	-0.49, 6.45	0.09	**2.37**	**0.13, 4.60**	**0.04**	2.00	-0.26, 4.26	0.08

Outcomes	Intervention N= 69		Routine-care N= 70		Unadjusted effect (95%CI)		P-value	Adjusted effect* (95%CI)		P-value*	Adjusted effect** (95%CI)		P-value**
Skinfold thickness (mm)‡													
- **Biceps**	10.5	5.8	10.1	4.4	0.39	-1.31, 2.08	0.66	0.20	-1.18, 1.57	0.78	0.10	-1.24, 1.44	0.89
- **Triceps**	23.5	8.3	23.3	7.9	0.17	-2.49, 2.84	0.90	-0.18	-2.42, 2.05	0.87	-0.62	-2.87, 1.63	0.59
- **Subscapular**	26.4	13.6	26.6	11.6	-0.13	-4.30, 4.03	0.95	0.93	-2.08, 3.95	0.54	0.60	-2.40, 3.61	0.69
- **Suprailiac**	21.7	11.1	23.2	11.0	-1.48	-5.11, 2.15	0.42	-1.72	-4.65, 1.20	0.25	-2.60	-5.40, 0.20	0.07
Central subcutaneous adiposity[1]	48.2	23.6	49.8	21.4	-1.61	-9.06, 5.83	0.67	-0.79	-6.23, 4.65	0.78	-2.00	-7.36, 3.37	0.47
Peripheral subcutaneous adiposity[2]	33.9	13.1	33.4	11.6	0.56	-3.53, 4.64	0.79	0.01	-3.21, 3.24	0.99	-0.53	-3.78, 2.72	0.75
Total subcutaneous adiposity[3]	82.1	35.4	83.2	31.2	-1.06	-12.07, 9.96	0.85	-0.78	-8.71, 7.16	0.85	-2.52	-10.37, 5.32	0.53
Subscapular-to-triceps ratio	1.1	0.4	1.2	0.5	-0.06	-0.20, 0.07	0.36	0.00	-0.13, 0.14	0.94	0.01	-0.13, 0.15	0.90
Central-to-total ratio[4]	57.3	6.7	58.5	7.8	-1.29	-3.69, 1.11	0.29	-0.28	-2.59, 2.02	0.81	-0.55	-2.89, 1.78	0.64

Figures are numbers and percentage, and treatment effects are relative risks (95% CI) for binary data and mean differences (95% CI) for continuous data unless otherwise indicated;

‡values are means (standard deviation), and effects are mean difference (95% CI).

†Primary outcome; *adjusted for baseline imbalances: in maternal BMI at first antenatal visit, smoking status, ethnicity, family history of diabetes and socioeconomic status. **Adjusted for baseline imbalances and potential confounders including centres, oral glucose challenge test result, gestational age at entry, age and parity; §Odds of having a higher BMI category at 4 months postpartum.

[1]Defined as a sum of suprailiac and subscapular skinfold thickness; [2]defined as a sum of triceps and biceps skinfold thickness; [3]defined as a sum of suprailiac, subscapular, triceps and biceps skinfold thickness; [4]defined as percentage of central subcutaneous adiposity to total subcutaneous adiposity.

NA: not applicable as there were too few outcome events for adjusted analysis.

difference was seen in infant head circumference z-score between the two study groups at follow-up in the unadjusted (245 infants, MD 0.00, 95% CI -0.27 to 0.27, p=1.00) or adjusted analyses (Table 6.3).

Of the 139 infants who provided four-month morphology outcome data, 69 were from the intervention group and 70 were from the control group. No significant difference was seen in ponderal index between infants born to women in the two study groups at four months of age in the unadjusted analysis (139 infants, MD -0.13 kg/m3, 95% CI -0.98 to 0.72, unadjusted p=0.76) or the adjusted analyses (Table 6.5). When compared with infants born to women in the routine-care group, those born to women in the intervention group had no significant differences in chest circumference (MD -0.37 cm, 95% CI -1.11 to 0.36, unadjusted p=0.32); arm circumference (MD -0.15 cm, 95% CI -0.57 to 0.26, unadjusted p=0.47); and abdomen circumference (MD -0.54 cm, 95% CI -1.54 to 0.45, unadjusted p=0.29) at four months of age in the unadjusted analysis or any of the respective adjusted analyses (Table 6.5).

Infants born to women who received diet and exercise intervention during pregnancy for managing borderline GDM had significantly smaller subscapular skinfold thickness (139 infants, MD -0.93 mm, 95% CI -1.69 to -0.17, unadjusted p=0.02) at four months of age when compared with infant born to women received standard antenatal care during pregnancy (Table 6.5). After adjustment was made for baseline imbalances and for both baseline imbalances and potential confounders, the differences remained significant (139 infants, adjusted for baseline imbalances: MD -0.88 mm, 95% CI -1.62 to -0.13, adjusted p=0.02; adjusted for baseline imbalances and potential confounders: MD -0.90 mm, 95% CI -1.65 to -0.15, adjusted p=0.02) (Table 6.5). No significant difference between the two study groups was seen in infant skinfold thickness measured

Table 6.5 Infant anthropometric outcomes at four months of age by treatment group

Outcomes	Intervention group N= 69		Routine-care group N= 70		Unadjusted effect (95%CI)			P-value	Adjusted effect* (95%CI)			P-value*	Adjusted effect** (95%CI)			P-value**
Ponderal Index (kg/m^3)	26.0	2.9	26.1	2.3	-0.13	-0.98,	0.72	0.76	-0.35	-1.26,	0.57	0.46	-0.26	-1.20,	0.68	0.59
Circumference (cm)																
- **Chest**	42.2	2.0	42.5	2.4	-0.37	-1.11,	0.36	0.32	-0.34	-1.13,	0.45	0.40	-0.27	-1.05,	0.51	0.50
- **Arm**	14.1	1.4	14.3	1.2	-0.15	-0.57,	0.26	0.47	-0.05	-0.49,	0.38	0.81	-0.05	-0.50,	0.39	0.82
- **Abdomen**	41.5	2.8	42.1	3.2	-0.54	-1.54,	0.45	0.29	-0.40	-1.48,	0.69	0.47	-0.22	-1.26,	0.81	0.67
Skinfold thickness (mm)																
- **Biceps**	5.4	1.3	5.7	1.4	-0.24	-0.68,	0.21	0.29	-0.25	-0.72,	0.21	0.28	-0.39	-0.83,	0.05	0.08
- **Triceps**	9.2	2.4	9.8	2.6	-0.57	-1.40,	0.26	0.18	-0.32	-1.18,	0.53	0.46	-0.32	-1.20,	0.56	0.48
- **Subscapular**	7.6	1.9	8.6	2.6	**-0.93**	**-1.69,**	**-0.17**	**0.02**	**-0.88**	**-1.62,**	**-0.13**	**0.02**	**-0.90**	**-1.65,**	**-0.15**	**0.02**
- **Suprailiac**	7.5	3.4	8.2	3.7	-0.67	-1.84,	0.50	0.26	-0.62	-1.82,	0.57	0.31	-0.74	-1.67,	0.19	0.12
- **Abdomen**	7.8	3.1	8.7	2.8	-0.86	-1.84,	0.12	0.09	-0.49	-1.51,	0.53	0.34	-0.51	-1.54,	0.53	0.34
- **Thigh**	18.8	4.3	20.0	4.6	-1.16	-2.62,	0.31	0.12	-1.11	-2.63,	0.42	0.15	-0.90	-2.40,	0.60	0.24
Central subcutaneous adiposity[1]	15.2	4.7	16.8	5.6	-1.60	-3.31,	0.10	0.07	-1.50	-3.18,	0.19	0.08	**-1.64**	**-3.11,**	**-0.17**	**0.03**
Peripheral subcutaneous adiposity[2]	14.7	3.3	15.5	3.7	-0.81	-1.97,	0.35	0.17	-0.58	-1.76,	0.61	0.34	-0.71	-1.92,	0.50	0.25
Total subcutaneous adiposity [3]	29.8	6.7	32.2	8.7	-2.41	-4.97,	0.15	0.07	-2.07	-4.59,	0.44	0.11	**-2.35**	**-4.73,**	**0.02**	**0.05**
Subscapular-to-triceps ratio	0.9	0.3	0.9	0.2	-0.02	-0.10,	0.07	0.71	-0.05	-0.13,	0.04	0.32	-0.05	-0.14,	0.03	0.22
Central-to-total ratio[4]	50.3	6.5	51.4	5.3	-1.12	-3.08,	0.83	0.26	-1.27	-3.34,	0.80	0.23	-1.30	-3.10,	0.51	0.16

Values are means (standard deviation), and effects are mean difference (95% CI). *Adjusted for baseline imbalances: in maternal BMI at first antenatal visit, smoking status, ethnicity, family history of diabetes and socioeconomic status; **adjusted for baseline imbalances and potential confounders: maternal BMI at first antenatal visit, smoking status, ethnicity, family history of diabetes, socioeconomic status, centres, oral glucose challenge test result, gestational age at entry, age and parity.

[1]Defined as a sum of suprailiac and subscapular skinfold thickness; [2]defined as a sum of triceps and biceps skinfold thickness; [3]defined as a sum of suprailiac, subscapular, triceps and biceps skinfold thickness; [4]defined as percentage of central subcutaneous adiposity to total subcutaneous adiposity.

at biceps, triceps, suprailiac area, abdomen and thigh at four-month follow-up in both unadjusted and adjusted analyses (Table 6.5).

There was no significant difference between the two study groups in infant central subcutaneous adiposity at four months of age in the unadjusted analysis (139 infants, MD -1.60 mm, 95% CI -3.31 to 0.10, unadjusted p=0.07) or the analysis adjusted for maternal baseline imbalances (Table 6.5). However, in the analysis adjusted for both maternal baseline imbalances and potential confounders, infants born to women in the intervention group had significantly less central subcutaneous adiposity when compared with those born to women in the routine-care group at four months of age (139 infants, MD -1.64 mm, 95% CI -3.11 to -0.17, adjusted p=0.03) (Table 6.5).

No significant difference between the two study groups was seen in infant total subcutaneous adiposity at four months of age in the unadjusted analysis (139 infants, MD -2.41, 95% CI -4.97 to 0.15, unadjusted p=0.07) or the analysis adjusted for maternal baseline imbalances (Table 6.5). However, in the analysis adjusted for both maternal baseline imbalances and potential confounders, infants born to women in the intervention group had borderline significantly less total subcutaneous adiposity at four months of age when compared with those born to women in the routine-care group (139 infants, MD -2.35 mm, 95% CI -4.73 to 0.02, adjusted p=0.05) (Table 6.5).

No significant differences were seen between the two groups in infant peripheral subcutaneous adiposity (139 infants, MD -0.81, 95% CI -1.97 to 0.35, unadjusted p=0.17), subscapular-to-triceps ratio (139 infants, MD -0.02, 95% CI -0.10 to 0.07, unadjusted p=0.71) or central-to-total subcutaneous adiposity ratio (139 infants, MD -1.12, 95% CI -3.08 to 0.83, unadjusted p=0.26) at four months of age in the unadjusted analysis or any of the respective adjusted analyses (Table 6.5).

6.4.4.2 Maternal outcomes

Of the 139 women who provided four-month postpartum morphology outcome data, 69 were from the intervention group and 70 were from the routine-care group. The incidence of women with excessive weight retention (4.5 kg or more heavier than their prepregnancy or early pregnancy weight) was 44.9% (31 women) for the intervention group and 47.1% (33 women) for the routine-care group. The difference between the two groups was not statistically significant in the unadjusted analyses (relative risk (RR) 0.95, 95% CI 0.66 to 1.37, unadjusted p=0.80) (Table 6.4). Similarly there was no significant difference between the two study groups in mean maternal BMI at four months postpartum in the unadjusted analysis (139 women, MD 1.33 kg/m2, 95% CI -0.30 to 2.95, p=0.11) or the adjusted analyses (Table 6.4).

In post-hoc analyses, maternal weight change between IDEAL trial entry and four months postpartum was not significantly different between the two study groups in the unadjusted analysis (139 women, MD -0.02 kg, 95% CI -1.93 to 1.89, p=0.98) or the adjusted analyses (Table 6.4). No significant difference was seen in mean maternal BMI change between IDEAL trial entry and four months postpartum between women in the intervention and routine-care group in the unadjusted analysis (139 women, MD -0.09 kg/m^2, 95% CI -0.84 to 0.65, unadjusted p=0.81) or the adjusted analyses (Table 6.4).

For maternal BMI categories of underweight (< 18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2) and obese (≥30 kg/m^2) at four months postpartum, the risk of being in a higher BMI category was not significantly different between the two study groups (139 women, OR 1.58, 95% CI 0.84 to 2.95, unadjusted p=0.15) (Table 6.4). Two (2.9%) women in the intervention group and no woman in the routine-care group were underweight (BMI <18.5 kg/m^2) at follow-up (Table 6.4). The proportion of women in the BMI category of overweight (BMI 25-29.9 kg/m^2) was 23.2%

for the intervention group and 28.6% for the routine-care group. There were another 22 (31.9%) women in the intervention group and 12 (17.1%) women in the routine-care group who were obese (BMI ≥30 kg/m^2) (Table 6.4). In a post-hoc analysis of maternal BMI category change between IDEAL trial entry and four months postpartum, there was no significant difference between the two study groups (Table 6.6).

In the adjusted or unadjusted analyses, women in the intervention group did not have significant differences in arm circumference (139 women, MD 0.00 cm, 95% CI -1.44 to 1.44, unadjusted p=1.00) or gluteal circumference (139 women, MD 2.05 cm, 95% CI -1.34 to 5.45, unadjusted p=0.24) at four months postpartum when compared with women in the routine-care group (Table 6.4). At four months postpartum, there was no significant difference in maternal waist circumference between the two study groups in the unadjusted analysis (139 women, MD 2.98 cm, 95% CI -0.49 to 6.45, unadjusted p=0.09) (Table 6.4). However, the difference in maternal waist circumference between groups reached statistical significance in the analysis that adjusted for maternal baseline imbalance (139 women, MD 2.37 cm, 95% CI 0.13 to 4.60, adjusted p=0.04). After further adjustment was made for potential confounders, this difference was no longer significant (139 women, MD 2.00 cm, 95% CI -0.26 to 4.26, adjusted p=0.08).

In the unadjusted or adjusted analyses, no significant differences were seen in maternal biceps skinfold thickness (139 women, MD 0.39 mm, 95% CI -1.31 to 2.08, unadjusted p=0.66); triceps skinfold thickness (139 women, MD 0.17 mm, 95% CI -2.49 to 2.84, unadjusted p=0.90); subscapular skinfold thickness (139 women, MD -0.13 mm, 95% CI -4.30 to 4.03, unadjusted p=0.95); or suprailiac skinfold thickness (139 women, MD -1.48 mm, 95% CI -5.11 to 2.15, unadjusted p=0.42) between women in the two study groups at four months postpartum (Table 6.4). There were no significant differences in maternal central subcutaneous adiposity (139 women, MD -1.61 mm, 95% CI -9.06 to

Table 6.6 Maternal BMI category change between IDEAL Trial entry and 4 months postpartum

BMI category	Intervention group (N=69)		Routine-care group (n=70)		P value
Trial entry: underweight (< 18.5 kg/m^2)	N=2		N=1		
4 months postpartum:					
Underweight	2	100.0	0	0.0	0.33*
Normal weight	0	0.0	1	100.0	
Trial entry: normal weight (18.5-24.9 kg/m^2)	N=38		N=45		
4 months postpartum:					
Normal weight	29	76.3	34	75.6	0.60*
Overweight	8	21.1	11	24.4	
Obese	1	2.6	0	0.0	
Trial entry: overweight (25-29.9 kg/m^2)	N=16		N=14		
4 months postpartum:					
Normal weight	0	0.0	2	14.3	0.23*
Overweight	8	50.0	8	57.1	
Obese	8	50.0	4	28.6	
Trial entry: obese (≥30 kg/m^2)	N=13		N=10		
4 months postpartum:					
Normal weight	0	0.0	1	10.0	0.18*
Overweight	0	0.0	1	10.0	
Obese	13	100.0	8	80.0	
Mother BMI category improved[1]	0	0.0	4	5.7	0.12*
Mother BMI category not changed	52	75.4	50	71.4	0.32**
Mother BMI category worse[2]	17	24.6	16	22.9	0.81

Figures are numbers and percentage.

*Fisher's exact test.

**Adjusted for baseline imbalances and potential confounders: maternal BMI at first antenatal visit, smoking status, ethnicity, family history of diabetes, socioeconomic status, centres, oral glucose challenge test result, gestational age at entry, age and parity.

[1]Defined as BMI category at 4-month postpartum lower than that at trial entry.

[2]Defined as BMI category at 4-month postpartum higher than that at trial entry.

BMI: body mass index

5.83, unadjusted p=0.67); peripheral subcutaneous adiposity (139 women, MD 0.56 mm, 95% CI -3.53 to 4.64, unadjusted p=0.79); total subcutaneous adiposity (139 women, MD -1.06 mm, 95% CI -12.07 to 9.96, unadjusted p=0.85); subscapular-to-triceps ratio (139 women, MD -0.06, 95% CI -0.20 to 0.07, unadjusted p=0.36) or central-to-total subcutaneous adiposity ratio (139 women, MD -1.29, 95% CI -3.69 to 1.11, unadjusted

p=0.29), or for any of the adjusted analyses, between women in the two study groups at four months postpartum (Table 6.4).

6.5 Discussion

Based on the outcome data provided by a randomised cohort of 245 mother and baby pairs, our study found that additional interventions, including diet and exercise advice and blood glucose monitoring during pregnancy for women with borderline GDM did not affect infant weight at four to 12 months of age. In keeping with the lack of effect observed, the incidence of infants' weight above the 90th centile or below the 10th centile and ponderal index did not differ. Although no change in circumferences of chest, arm and abdomen at follow-up was seen, the lifestyle interventions did reduce children's subcutaneous adiposity. Infants born to women with borderline GDM who received additional diet and exercise interventions during pregnancy had smaller subscapular skinfold thickness and less central and total subcutaneous adiposity at four months of age when compared with those born to women who received standard antenatal care. The subscapular z-score is 7.5 mm for both girls and boys at four months of age (WHO 2007). In our study, infants born to women with borderline GDM who received additional lifestyle interventions had a mean subscapular skinfold thickness of 7.6 mm, which is close to the average subscapular z-score; while infants born to women with borderline GDM who received routine-care had larger subscapular skinfold thicknesses of 8.6 mm at four months of age.

The relationship between body fat distribution and health outcomes in paediatric population has been studied in previous non-randomised studies (Crowther et al 1998; Madsen et al 2010; Maffeis et al 2001; Ramos-Arellano et al 2011; Slining et al 2010). In a longitudinal study, Slining and colleagues followed 215 infants at three, six, nine,

12 and 18 months of age to investigate the relationship between being overweight, having high subcutaneous fat and motor development (Slining et al 2010). Results from longitudinal regression models adjusted for infant age and sex suggested infants with high subcutaneous fat, defined as the sum of subscapular, triceps and abdominal skinfold thickness above 90th percentile of the study population's age- and sex-specific skinfold distribution, were more than twice as likely as infants with lower subcutaneous fat to experience motor development delay at three to 18 months of age (Slining et al 2010). However, as infants involved in this study were from low-income families, with high risk of being overweight, the research findings may not apply to infants from a different population with higher socioeconomic status.

Based on the outcome data from a cohort of 265 nine-month-old infants, Madsen and colleagues found infant 2-hour fasting venous glucose concentration was positively associated with subscapular skinfold and the sum of subscapular and triceps skinfold thickness at nine months of age (Madsen et al 2010). Similarly, Crowther and colleagues found glucose and insulin concentrations at 30 minutes after an oral glucose tolerance test in children aged five years were positively associated with subscapular skinfold thickness (Crowther et al 1998).

In another cohort of 252 children in Mexico with an age range of six to 13 years, Ramos-Arellano and colleagues found hypertension, defined as systolic or diastolic blood pressure on the 95th percentile or higher in the children, was associated with high suprailiac skinfold, triceps skinfold and biceps skinfold after adjusting for age, sex and body mass index (Ramos-Arellano et al 2011). In prepubertal children aged three to 11 years, evidence from 818 children suggested cardiovascular risk factors, including adverse lipid profile and hypertension, were significantly associated with larger waist

circumference, triceps and subscapular skinfolds, and the relationship was independent of age, gender, and body mass index (Maffeis et al 2001).

In our study, lifestyle intervention for women with borderline GDM during pregnancy was associated with a reduction in the offspring's central subcutaneous body fat and overall adiposity during early infancy. A reduction in subcutaneous adiposity in early infancy may result in a reduced subcutaneous fat mass in early childhood (Ay et al 2008). This may lead to significant health benefits in later life by reducing the risks of motor development delay, or the development of cardiovascular disease and metabolic disorders (Crowther et al 1998; Madsen et al 2010; Maffeis et al 2001; Ramos-Arellano et al 2011; Slining et al 2010).

At four months postpartum, we found additional lifestyle interventions during pregnancy for women with borderline GDM did not affect maternal weight retention or their body fat distribution. Evidence from a previous systematic review of randomised trials involving women who are normal weight, overweight or obese at trial entry, has suggested diet and exercise interventions started early in pregnancy with regular follow-ups were effective in reducing maternal weight retention at six months postpartum, but had no impact on weight retention at six weeks postpartum (Tanentsapf et al 2011). Diet and exercise counselling provided after childbirth for women who were overweight, obese or gained excessive weight during pregnancy was also found to be effective in reducing maternal body fat, assisting postpartum weight loss and helping women to return to their prepregancy weight (Amorim Adegboye and Linne 2013).

In our study, only 8 (11.6%) women in the intervention group and 11 (15.7%) women in the routine-care group returned to within 1 kg of their prepregnancy or early pregnancy weight by four months postpartum. In the study conducted by Lovelady and colleagues, 40 women who were overweight at four weeks postpartum were randomised to receive

diet and exercise interventions for 10 weeks or maintain their usual diet and exercise (Lovelady et al 2000). By 14 weeks postpartum, 10 (48%) women in intervention group and 4 (21%) women in the routine-care group were within 1 kg of their prepregnancy weight (Lovelady et al 2000). Leermakers and colleagues recruited 90 women who had given birth in the past three to 12 months and whose weight exceeded their pre-pregnancy weight by at least 6.8 kg (Leermakers et al 1998). By the end of the 6-month study period, 12 (33%) women in the group having diet and exercise interventions but only 3 (11.5%) women in the group receiving standard care had returned to their prepregnancy weight (Leermakers et al 1998). In the study conducted by Ferrara and colleagues, 197 women with GDM were randomised to receive either diet and exercise interventions started during pregnancy and continued until 12 months postpartum or standard care (Ferrara et al 2011). The goal for women's weight management was to return to their prepregnancy weight, if it was normal, or achieve a 5% reduction from prepregnancy weight if overweight (Ferrara et al 2011). In this study, there was no significant difference in the proportion of women achieving their weight management goals at six weeks postpartum, seven months postpartum or 12 months postpartum between the two study groups (Ferrara et al 2011). However, the proportion of women achieving their weight management goals in this study reported for all the three time points was higher than we found for the cohort of women in our study at four months postpartum (Ferrara et al 2011). Ferrara and colleagues found that, the proportions of women who had achieved their weight goals were 19 (20.9%) women in the intervention group and 17 (17.4%) women in the routine-care group by six weeks postpartum; 27 (38%) women in the intervention group and 21 (23.9%) women in the routine-care group by seven months postpartum; 27 (37.5%) women in the intervention group and 18 (21.4%) women in the routine-care group by 12 months postpartum (Ferrara et al 2011).

It is unclear whether the null findings for maternal outcomes in our study and relatively low percentage of women who returned to their prepregnancy or early pregnancy weight relate to the population studied, the study intervention (i.e. duration, intensity and compliance) or the time when the postpartum assessment was carried out.

Three previous randomised trials have been conducted to assess the effects of intensive management including diet counselling, blood glucose monitoring or insulin therapy compared with standard antenatal care for women with mild pregnancy hyperglycaemia not meeting GDM diagnostic criteria (Bevier et al 1999; Bonomo et al 2005; Langer et al 1989) (as presented within Cochrane systematic review in Chapter 4 of this thesis). Evidence from these three randomised trials involved 509 women suggested intensive management of very mild pregnancy hyperglycaemia was effective in reducing macrosomic and large-for-gestational-age babies, but had no impact on maternal pregnancy weight gain (Han et al 2012a). None of these studies however reported outcomes for women and their babies beyond birth (Bevier et al 1999; Bonomo et al 2005; Langer et al 1989).

Large, well-designed randomised trials have suggested that management of mild GDM through dietary advice and insulin therapy compared with standard pregnancy care reduced the risk of being macrosomia and large-for-gestational-age, and was associated with less pregnancy weight gain (Crowther et al 2005; Landon et al 2009). However, longer-term outcomes for women and their babies involved in these two completed randomised trials have been limited. Longer term outcomes for only a small subset of 199 children at 4-5 years of age born to women recruited to the ACHOIS randomised trial have been reported (Crowther et al 2005), with no significant difference seen between groups in the incidence of child BMI above the 85th centile (Gillman et al 2010).

Overall, the evidence on longer-term effects of interventions for managing pregnancy hyperglycaemia of various severities during pregnancy is very limited. We did not locate any similar studies with which to compare our nested In-depth early Follow-Up Study of women and babies within the IDEAL Trial.

6.5.1 **Strengths and limitations of this study**

The major strength of our study is that the women and their babies were from a randomised trial, most baseline characteristics were matched, enabling valid comparisons to assess longer-term effects of this diet and exercise intervention during pregnancy. In addition, follow-up assessments in our study were carried out by research staff that were unaware of group allocation, which reduced the risk of performance bias.

Our study is limited by the fact that we were only able to follow up only a proportion of the total IDEAL cohort. However, women involved in the In-depth Follow-Up Study had similar baseline characteristics of women involved in the IDEAL main trial and any imbalances in maternal baseline characteristics identified in our study were adjusted for in the analyses. Given the multiple testing used in our study, it is possible that some results were significant due to chance. However, we found a consistent trend that infant born to women receiving routine-care had higher adiposity than those born to women in the intervention group at four months of age. Measurement error in the present study may be inevitable while measuring weight, height, circumferences and skinfold thickness. To minimise performance bias, we used a standard protocol and assessors were trained before taking assessment. Moreover, multiple measurements were taken for each measurement and mean values were used in analyses.

Previous observational studies have suggested mild pregnancy hyperglycaemia was associated with an increased risk of metabolic disorders for both women and their

babies at different postpartum periods and ages (Clausen et al 2008; Retnakaran et al 2010; Silverman et al 1995; Stuebe et al 2011). Unfortunately, our study did not have funding to assess the metabolic impact of management for women with borderline GDM on maternal and child metabolic outcomes in the early postnatal period.

6.6 Conclusions

6.6.1 **Implications for clinical practice**

Our study found additional lifestyle interventions during pregnancy for women with borderline GDM did not change women's weight retention at four months postpartum or their children's weight at 4 to 12 months of age, but did reduce the children's central and overall subcutaneous body fat. It is important to note that our findings were based on evidence from a relatively small proportion of the randomised cohort from the IDEAL Trial assessed, early in the postnatal period. The main IDEAL Trial is still to report its findings. Until additional evidence from larger and longer-term follow-up studies of well-designed randomised trials becomes available, current evidence from this nested In-depth Follow-Up Study within the IDEAL Trial is insufficient to make recommendations on overall management for women with borderline GDM.

6.6.2 **Implications for research**

Longer-term follow-up studies of women and children who were involved in the completed randomised trials assessing interventions for managing pregnancy hyperglycaemia are warranted. One such cohort is the women and babies from the IDEAL trial.

Based on the limited evidence from previous observational studies and given the findings of differences in infant body fat distribution seen in this study, a follow-up

study of children from the whole IDEAL study at prepubertal age (i.e. three- to six-years old, and/or 11- to 13- years old) is needed. It is important to see whether the reduction in the children's central and overall subcutaneous adiposity observed in early infancy persists into later life and whether there is any difference between children from the two study groups in growth patterns beyond early infancy. Moreover, outcomes such as children's motor development in early childhood, blood glucose concentrations, blood lipids profile and blood pressure need to be considered during a longer-term follow-up study.

For women, it is important to include outcomes such as maternal weight and body composition and metabolic outcomes in future longer-term follow-up studies. To achieve a better understanding of the effect of lifestyle intervention on the longer-term health outcomes of women, women's adherence to diet and exercise interventions needs to be assessed during the follow-up period.

7 Summary conclusions

7.1 Conclusions from the three Cochrane systematic reviews on pregnancy hyperglycaemia

In Chapters 2, 3 and 4 of this thesis, we systematically reviewed evidence from randomised controlled trials relating to the three research gaps identified in my literature review and have published the results in the Cochrane Library during the time course of this thesis (Han et al 2012a; Han et al 2013; Han et al 2012b).

For the research gap on the effects of exercise during pregnancy for preventing gestational diabetes mellitus (GDM), a Cochrane systematic review entitled "Exercise for pregnant women for preventing gestational diabetes mellitus" was conducted (Han et al 2012a). Based on evidence from five randomised controlled trials involving 922 women and their babies, we did not find a significant difference in GDM incidence between women receiving additional exercise interventions and routine care (Han et al 2012a). Implications for future clinical practice and research are summarised in Table 7.1.

For the research gap on the different types of dietary advice for women with GDM, we conducted a Cochrane systematic review of "Different types of dietary advice for women with gestational diabetes mellitus" (Han et al 2013). Nine randomised controlled trials involving 429 women and 436 babies were included (Han et al 2013). Eleven different types of diet were assessed under six different comparisons, including low-moderate glycaemic index (GI) food versus high-moderate GI food, low-GI diet versus high-fibre, moderate GI diet, energy restricted diet versus no energy restriction

Table 7.1 Summary of '*Exercise for pregnant women for preventing gestational diabetes mellitus*' Cochrane systematic review

Included studies	• Five randomised controlled trials (922 women and their babies) – as of 2 April 2012.
Interventions and comparisons	• Intervention group: additional regular exercise advice or stationary cycling sessions. • Control group: routine obstetric care.
Risk of bias of included studies	• Moderate risk of bias overall.
Findings	• No significant difference in GDM incidence between women receiving additional exercise interventions and routine care.
Implications for clinical practice	• Limited and incomplete body of evidence from randomised trials. • Insufficient to inform or guide practice.
Implications for research	• Further well-designed trials with sufficient power are needed. • Several such trials are in progress. • Different types and intensities of exercise interventions should be compared. • Outcomes such as longer-term health outcomes for women and their children and health service costs should be included.

Source: (Han et al 2012b)

diet, low carbohydrate diet (≤ 45% daily total energy intake from carbohydrate) versus high carbohydrate diet (≥ 50% daily total energy intake from carbohydrate), high monounsaturated fat diet (at least 20% total energy from monounsaturated fat) versus high carbohydrate diet (at least 50% total energy from carbohydrate) and standard fibre diet (20 g fibre/day) versus fibre enriched diet (80 g fibre/day) (Han et al 2012a).

We did not find any one type of dietary advice was more effective than others in reducing the risk of caesarean section, operative vaginal birth, large for gestational age

or macrosomic infants (Han et al 2012a). Implications for future clinical practice and research are summarised in Table 7.2.

Table 7.2 Summary of '*Different types of dietary advice for women with gestational diabetes mellitus'* Cochrane systematic review

Included studies	• Nine randomised controlled trials involving 429 women and 436 babies - as of 17 April 2012. • Eleven different types of diet were assessed under six different comparisons.
Risk of bias of included studies	• Various levels of risk of bias.
Findings	• We did not find any significant differences between any diets compared with another diet.
Implications for clinical practice	• Very limited number of trials, participants and data available for each of the six dietary comparisons. • No conclusive suggestions on the most appropriate diets for women with GDM can be made.
Implications for research	• Further larger trials with sufficient power are needed. • No ongoing trials identified. • Participants' adherence to dietary interventions and methods about improving intervention adherence need to be addressed and reported. • Multi-faceted dietary interventions (i.e. a dietary intervention targeting total energy, proportion of energy from different macronutrients and glycaemic index) may be worth considering. • Outcomes such as longer-term health outcomes for women and their babies, women's quality of life and health service cost should be included.

Source: (Han et al 2013)

A third Cochrane systematic entitled "Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria" was conducted to address the research gap on the different interventions for women with mild pregnancy hyperglycaemia (Han et al 2012b). We included four randomised controlled trials involving 521 women and their babies and found women receiving interventions were less likely to have macrosomic or large for gestational age babies without increased risk of caesarean section or operative vaginal birth (Han et al 2012b). Implications for future clinical practice and research are summarised in Table 7.3.

Although the currently available evidence offers only limited guidance for clinical practice, a number of potentially relevant trials will soon be completed and will widen the evidence base in some areas (Crowther et al 2012; Wolever 2010). The intent is for the Cochrane systematic reviews to be updated as new information from trials becomes available.

Given the increasing prevalence of GDM around the world and its implication for the short- and long-term health outcomes for women and their babies, further research into preventing and managing pregnancy hyperglycaemia remains a high priority.

Table 7.3 Summary of *'Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria'* Cochrane systematic review

Included studies	• Four randomised controlled trials included involving 521 women and their babies.
Interventions and comparisons	• Intervention group: dietary advice providing 24-30 kcal/ kg/ day based on prepregnancy weight or dietary advice to choose low glycaemic index food. • Control group: routine obstetric care, habitual diet without specific dietary interventions.
Risk of bias of included studies	• Three trials were at moderate to high risk of bias and one trial was at low to moderate risk of bias.
Findings	• Women receiving interventions were less likely to have macrosomic or large for gestational age babies without increased risk of caesarean section or operative vaginal birth.
Implications for clinical practice	• Limited evidence from small randomised trials. • Suggestion of benefits (reduced incidence of macrosomic and large for gestational age babies) by providing interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria. • However, current evidence is not sufficient to change current clinical practice.
Implications for research	• Further larger trials with sufficient power are needed • Two such trials are ongoing. • Outcomes such as longer-term health outcomes for women and their babies and health service cost should be included.

Source: (Han et al 2012a)

7.2 Conclusions from the qualitative semi-structured interview study

In Chapter 5, research findings were presented from a qualitative study exploring women's experiences after being diagnosed with borderline gestational diabetes mellitus (GDM), their attitudes about treatment, and factors important to them for achieving any lifestyle changes. Research findings of this qualitative study are summarised in Table 7.4.

Table 7.4 Summary of the research findings for the qualitative semi-structured interview study

Participants	22 women were interviewed.
Feelings after a diagnosis of borderline GDM	Caused some concern to one third of women interviewed.
Women's attitudes about providing management for borderline GDM	95% women rated management as important or very important, one woman (5%) was unsure.
Helpers for women to achieve intended lifestyle changes	• A wide range of factors were reported. • Thinking about baby's health and their own health were the most important facilitators.
Inhibitors for women to achieve intended lifestyle changes	• Varied greatly. • The three most frequently mentioned inhibitors were being physically unwell, busy life, and inadequate family support.
Needs to overcome barriers	• Varied greatly, depending on the barriers that women experienced. • The most frequently mentioned needs were better family support from partners and/or parents.

A diagnosis of borderline GDM caused some concern for one third of women interviewed. The majority of women believed managing their borderline GDM was

important and they planned to improve their lifestyle. Although women nominated many different factors that might influence their lifestyle choices, their own and their baby's future health were powerful motivators for change and the most significant barrier was a lack of family support (Table 7.4).

As the first qualitative semi-structured interview study targeting women with borderline GDM, our work provides further understanding of women's views and experiences in dealing with a diagnosis of borderline GDM and the subsequent management requirements. It also provides important information on factors that may affect women's ability to achieve their intended lifestyle modifications. These research findings may help with designing and delivering future health care that meets the individual needs of women with pregnancy hyperglycaemia.

7.3 Conclusion for the In-depth IDEAL 4 to 12 month Follow-Up Study

In Chapter 6, research findings were presented from the In-depth IDEAL 4 to 12 month Follow-Up Study. Details of this Follow-Up Study are summarised in Table 7.5.

Based on the evidence from 245 mother-baby pairs involved in the IDEAL randomised Trial, our study found additional interventions, including diet and exercise advice and blood glucose monitoring during pregnancy for women with borderline GDM, had no impact on maternal weight retention at four months postpartum. Their babies' weight at 4 to 12 months of age was not influenced nor any of the secondary outcomes except infant subcutaneous adiposity at four months of age. Infants born to women who received additional lifestyle interventions when compared with those infants born to women who received routine-care had smaller subscapular skinfold thickness, sum of

Table 7.5 Summary of the research findings for the In-depth IDEAL 4 to 12 month Follow-Up Study

	Intervention group	**Routine-care group**
Participants	121 mother-baby pairs	124 mother-baby pairs
Interventions and comparisons in the IDEAL Trial	• Standard antenatal care • Diet and exercise advice • Blood glucose monitoring	• Standard antenatal care
Outcomes	**Primary outcomes:** • Infant weight z-score at follow-up. • Maternal weight within 1kg of prepregnancy/ early pregnancy weight at 4 months postpartum. **Secondary outcomes:** • Comprehensive maternal and child anthropometric outcomes, including body fat distribution.	
Results	• No significant difference between the two study groups in infant weight z-score and the incidence of women within 1 kg of their prepregnancy or early pregnancy weight at follow-up. • Infants born to women who received additional lifestyle intervention had significantly smaller subscapular skinfold thickness and less central and total subcutaneous adiposity at four months of age when compared with those born to women received routine-care. • No differences were seen in other prespecified maternal and child secondary outcomes.	
Implications for clinical practice	• Current evidence is insufficient to make conclusive recommendation on management for women with borderline GDM.	
Implications for research	• Longer-term follow-up studies of women and children involved in completed randomised trials are needed. • One such cohort is the women and children in the IDEAL randomised trial. • Outcomes such as maternal and child body adiposity and long-term metabolic outcomes should be included.	

suprailiac and subscapular skinfold thickness, and sum of suprailiac, subscapular, triceps and biceps skinfold thickness.

Our study is the first randomised trial that has reported health outcomes beyond birth for women and their babies assessing the effect of lifestyle intervention for managing borderline GDM. Future longer-term follow-up studies are needed to investigate whether lifestyle interventions during pregnancy for managing borderline GDM have any continuing impact on women and their babies' health, such as maternal and child body composition and metabolic outcomes in later life. Following up the unique cohort of women and their babies involved in the IDEAL randomised trial in the longer term will provide important information to help answer these on-going research questions.

7.4 Overall conclusions

This thesis presented evidence from research studies aimed to investigate and evaluate the strategies used for preventing, diagnosing and managing pregnancy hyperglycaemia. Research methodologies used in this thesis included Cochrane systematic review, qualitative semi-structured interviews and an In-depth Follow-Up Study of women and babies involved in the IDEAL randomised trial.

Based on research findings presented in this thesis, it is clear that currently available evidence in the areas of preventing and managing pregnancy hyperglycaemia is incomplete and can provide only limited information to guide clinical practice. Areas for future research have been summarised earlier in this chapter, specifically relating to exercise for preventing GDM, types of dietary advice for women with GDM and interventions for pregnant women with hyperglycaemia not meeting GDM diagnostic criteria. Future studies must consider long-term health outcomes of women and their children when evaluating the effectiveness of study interventions.

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9 Appendix

9.1 Semi-structured question list used in interviews

1. What were your first impressions when you were told that you had borderline GDM?
2. How important do you think it is to provide management for borderline GDM? (Scale: very important, important, no sure, not very important)
3. Besides the information provided by the IDEAL study, did you seek other information about managing borderline GDM?
4. Since been involved in the IDEAL study, have you thought about making some changes to your diet or exercise to improve health?
5. What changes in your diet or exercise did you try and continue with?
6. What helped you achieve the success?
7. What changes did you try but could not continue?
8. What factors made it hard to continue?
9. Is there anything that could help?